COVERING LETTER

TO,

The Dean,

IHEC-PGR, AIIMS BHOPAL

Respected Sir,

SUB: SUBMISSION OF THESIS

I, Dr. Ajitendra Pratap Singh, who have joined the Department of Orthopaedics, AIIMS Bhopal as a Post Graduate in **July 2022 session** with Registration number : **2200438M02P31011.**

I am hereby submitting my thesis Titled "**Outcomes of Core Decompression with Bisphosphonate Versus Bisphosphonate Alone in Patients with Early Osteonecrosis of the Femoral Head; A Comparative Observational Study**" for your kind approval.

Thanking you

Yours sincerely,

Dr. Ajitendra Pratap Singh

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10/11/24

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"OUTCOMES OF CORE DECOMPRESSION WITH BISPHOSPHONATE VERSUS BISPHOSPHONATE ALONE IN PATIENTS WITH EARLY OSTEONECROSIS OF THE FEMORAL HEAD; A COMPARATIVE OBSERVATIONAL STUDY"

A thesis submitted to the faculty of

ALL INDIA INSTITUTE OF MEDICAL SCIENCES, BHOPAL

For the award of the degree MS in the subject of

Orthopaedics

By

Dr. Ajitendra Pratap Singh

(Reg No: 2200438M02P31011)

Under the guidance of

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(Oct 2024)

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I, **Dr. Ajitendra Pratap Singh ,** MS scholar registered in the batch **July 2022** with **Registration No:** 2200438M02P31011 hereby declare that the data submitted for my MS thesis belongs to me and it is original. I also certify that the work was done by me to carry out this study.

The Institute shall not be responsible for any dispute or any conflict of interest that may arise out of this thesis at any stage.

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by Ajitendra Pratap Singh

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Letter of Permission

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AIIMS, Bhopal Institutional Human Ethics Committee- Student Research (IHEC-SR) in its 7th meeting held on 22nd February 2023 discussed your proposal titled **"Outcomes of Core Decompression with Bisphosphonate versus Bisphosphonate alone in Patients with early Osteonecrosis of the Femoral Head; A Comparative Observational Study "** and evaluated it for suitability for your dissertation as required for fulfilment of MD/MS program.

Following members attended the meeting:

1. Prof. D. K. Pal, Former HoD Community Medicine, GMC, Bhopal……..…*Chairperson*
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The decision of the committee is as follows:

The AIIMS, Bhopal IHEC-SR approves your research protocol. All research related activities must begin only after the date of this approval. The validity of this approval is till two years from the date of issuance. Please submit a closure report / renewal request before expiration of the validity for this approval.

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List of Abbreviations

S. No.	ESWT	Extracorporeal Shockwave Therapy
1	HBOT	Hyperbaric Oxygen Therapy
2	ONFH	Osteonecrosis Of The Femoral Head
3	THA	Total Hip Arthroplasty
4	OFH	Osteonecrosis Of The Femoral Head
5	PPAR-γ	Peroxisome Proliferator–Activated Receptor Gamma
6	HIV	Human Immunodeficiency Virus
7	NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
8	PEFT	Pulsed Electromagnetic Field Therapy
9	HBO	Hyperbaric Oxygen
10	PRP	Platelet-Rich Plasma
11	HHS	Harris Hip Scores
12	OA	Osteoarthritis
13	CT	Computerized Tomography
14	MRI	Magnetic Resonance Imaging
15	ARCO	Association Research Circulation Osseous
16	HOOS	Hip Disability And Osteoarthritis Outcome Score
17	THR	Total Hip Replacement
18	JIC	Japanese Investigation Committee
19	MCID	Minimum Clinically Important Difference
20	S.D.	Standard Deviation

21	C.I.	Confidence Interval
22	SLE	Systemic Lupus Erythematosus
23	NCCT	Non Contrast Computed Tomography
24	VAS	Visual Analogue Score
25	NRS	Numeric Rating Scale
26	IBM-SPSS	International Business Machines Corporation – Statistical Package For The Social Sciences
27	AVN	Avascular Necrosis

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INTRODUCTION

INTRODUCTION

Osteonecrosis is a degenerative bone disorder marked by the death of bone cells due to a disruption in the blood flow to the subchondral region [1]. It is also referred to as avascular necrosis, aseptic necrosis, or ischemic bone necrosis. The condition primarily affects the epiphysis of long bones in weight-bearing joints. In severe cases, it can result in the destruction of subchondral bone or cause the collapse of the affected joint[1] Osteonecrosis most frequently occurs in the femoral head, knee, talus, and humeral head, with the hip being the most common site overall [2]

There are various risk factors and theories regarding the development of vascular impairment leading to osteonecrosis. Shah et al. concisely classify them into six categories.[3] These are:**Direct cellular toxicity** like chemotherapy, radiotherapy, thermal injury and smoking, **Extra osseous arterial fracture** seen in hip dislocation, femoral neck fracture, iatrogenic fracture post-surgery and lastly congenital arterial abnormalities, **Extra osseous venous** abnormalities and Venous stasis, **Intraosseous extravascular compression** like haemorrhage, elevated bone marrow pressure, fatty infiltration of bone marrow due to prolonged high-dose corticosteroid use, cellular hypertrophy and marrow infiltration (seen in Gaucher's disease), bone marrow oedema and displaced fractures and **Intraosseous intravascular occlusion** which includes coagulation disorders such as thrombophilia, hypo fibrinolysis and sickle cell crises and **Multifactorial**.[3]

I

Treatment options can be broken down into non-operative and operative categories. **Non-operative Treatment (Stages 0-2)** includes a) Bisphosphonates[4] b) Iloprost, a vasoactive prostaglandin [5][6] c)Statin therapy [7]to prevent corticosteroid-induced osteonecrosis d)Extracorporeal shockwave therapy (ESWT)[8][9] e)Hyperbaric oxygen therapy (HBOT) [10][11] e)Conservative measures including limited weight bearing with crutches, and pain medications. **Operative Treatment (Stages 3-4)** includes a) Core decompression [12] b) bone grafting[13] c) osteotomy [14] d)total hip arthroplasty[15] e) stem cell therapy[16][17][18][19] etc.

In treating osteonecrosis of the femoral head (ONFH), core decompression is employed during the early pre-collapse stages of the disease to delay or prevent the need for total hip arthroplasty (THA). The optimal candidate for this procedure is a small pre-collapse lesion (<15% of the femoral head or a Kerboul angle <200°) [20-23]. These procedures are typically carried out by drilling and extracting an 8 to 10 mm cylindrical core from the osteonecrotic lesion. [24] In addition, another commonly used technique involves multiple percutaneous drillings [24, 25]. These techniques are often combined with various adjunctive treatments, including bone grafting and the incorporation of growth and differentiation factors. [26-31]. Yoon et al. [20] assessed the impact of disease stage and lesion location on outcomes in 39 hips. After a mean follow-up of 61 months, they found that patients with Ficat stage II or III disease (17 out of 22 hips) were significantly more likely to require total hip arthroplasty (THA) compared to those with stage I disease (5 out of 17 hips) ($p < 0.001$). Furthermore, lesions located laterally or centrally had a significantly higher rate of conversion to THA

compared to those with medial lesions ($p = 0.009$). They also observed that larger lesions (>30% of the femoral head) were more likely to result in clinical failure ($p < 0.001$). The study concluded that the ideal candidate for core decompression is someone with pre-collapse disease and lesions less than 15% of the femoral head.

Bisphosphonates, like alendronate, induce osteoclast apoptosis through various mechanisms, including the inhibition of protein prenylation and the disruption of mevalonate metabolism [32]. Bisphosphonates reduce edema and slow the rate of bone remodeling, which helps shrink the remodeling spaces and prevent the progression of bone collapse [33]. Bone formed during alendronate treatment is histologically normal [34][35][36][37] and the treatment appears to offer the greatest protection against fracture A systematic review of eight studies involving 788 hips indicated that alendronate is effective in the short term for reducing pain, improving joint function, slowing the progression of bone collapse, and delaying the need for total hip arthroplasty in adults with osteonecrosis. [38].
Bisphosphonates are primarily used for non-operative management in patients with early-stage hip osteonecrosis who prefer to avoid surgical treatment [4]

Ours being a tertiary care institute most patients who presents with grade 1 or 2 osteonecrosis of femur head are already on some form of medical management especially bisphosphonates. All these patients are offered core decompression as a surgical option. However some of them refuse surgery leading to the creation of two groups: one treated with core decompression and

bisphosphonate therapy, and the other with bisphosphonate therapy alone. To the best of our knowledge, no previous studies have compared clinical, radiological, and patient-reported outcomes between these two treatment approaches, and our findings contribute to this ongoing debate about the best management strategies for osteonecrosis.

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REVIEW OF LITERATURE

REVIEW OF LITERATURE

Osteonecrosis of the femoral head (OFH) is a debilitating condition that commonly impacts individuals in their third to fifth decades of life [39]. As the femoral head collapses, it leads to pain and a decrease in function [40]. The natural course of the disease ultimately leads to complete collapse of the hip joint and arthritis, making early diagnosis and intervention crucial. However, in some cases, the disease progresses slowly, and clinical symptoms may remain stable for extended periods[41]. OFH is one of the leading causes of hip arthritis in middle-aged individuals, alongside hip dysplasia and femoroacetabular impingement. If left untreated, it often leads to severe secondary joint destruction in most patients. Although its incidence and prevalence are lower than those of primary osteoarthritis, OFH has a substantial economic impact due to its significant effect on the younger population. Therefore, early diagnosis and stage-appropriate treatment of OFH are crucial to preventing both primary and secondary joint damage

Etiology and Pathogenesis

While the exact etiology of OFH remains unclear, it is understood to result from a multifactorial process[42]. Long-term corticosteroid use is the most common risk factor and is the primary cause of OFH in 10 to 30% of cases. [43-55]. A treatment duration of two to three months with a daily dose of 2 grams or more of prednisolone (or its equivalent) is considered critical [44]. The pathophysiology of steroid-induced OFH remains controversial, with several mechanisms proposed. These include abnormalities in the bone marrow stem cell pool, hyperlipidemia, fat emboli distribution in circulation, a hypercoagulable state, vascular endothelial dysfunction, and

apoptosis of bone tissue. Research has shown that corticosteroid exposure leads to disruptions in lipid metabolism in both humans and animals. [46-50]. Steroid-associated OFH results from a combination of multiple factors rather than a single cause. These factors interact with each other throughout the development of osteonecrosis, ultimately leading to marrow ischemia and, eventually, osteonecrosis.

Excessive alcohol consumption is another significant contributor to the incidence of non-traumatic OFH. In a prospective study, Matsuo K et al. demonstrated that consuming up to 320 grams of ethanol per week (roughly equivalent to five bottles of wine) increased the risk of non-traumatic OFH by approximately 2.8 times [51]. Alcohol significantly affects serum triglyceride and cholesterol levels, as well as bone marrow fatty infiltration. In the subchondral regions of the femoral head, hypertrophy and proliferation of fat cells have been observed.

The deposition of triglycerides in osteocytes leads to pyknosis and an increased percentage of empty osteocyte lacunae. Similar to corticosteroids, alcohol promotes adipogenesis while inhibiting osteogenesis. However, in stromal cells treated with alcohol, there was no observed increase in Peroxisome proliferator–activated receptor gamma (PPAR-γ) expression, unlike the increase seen in steroid-treated cells. This suggests that alcohol affects fatty acid metabolism through a distinct mechanism. [52,53]. Both steroids and alcohol promote adipogenesis at the expense of osteoblastic proliferation and function. While the role of genetic predisposition in these patients has not been fully established, it may help explain why some chronic users of steroids or alcohol do not develop the disease [54].

Smoking has also been identified as a risk factor for OFH, although, unlike alcohol abuse, no clear dose-response relationship has been established. Both current and former smokers have a higher risk of developing OFH compared to non-smokers. Among smokers, those who smoke more than 20 cigarettes per day are at a greater risk than light smokers (fewer than 20 cigarettes per day), who in turn have a higher risk than non-smokers [51,55,56].

Jones JP Jr. proposed that hypercoagulability, particularly intravascular coagulation, could be a contributing factor to the development of OFH [57]. Thrombotic occlusion of the microcirculation can result from hereditary thrombophilia, impaired fibrinolysis, or the presence of antiphospholipid antibodies [58].

Other contributing factors include environmental or acquired conditions, such as hyperlipidemia, hypersensitivity reactions, thromboplastin release during pregnancy, malignant tumors, and inflammatory bowel disease. These factors may further increase the risk for individuals with an underlying genetic predisposition to form microvascular thrombi [59,60]. Intravascular coagulation appears to be a key mechanism in the pathogenesis of OFH in sickle cell disease and other hemoglobinopathies [61-63]. Björkman A et al., in a retrospective study of 63 adult patients with OFH, found that mutations in the factor V Leiden or prothrombin 20210A gene were significantly more common in patients with idiopathic OFH than in those with steroid- or alcohol-induced OFH, as well as in a healthy control population [64]. Zalavras and colleagues also found that the factor V Leiden mutation was present in 18% of 72 adult Caucasian patients with OFH, compared to 4.6% in 300 healthy control subjects[65]. Additionally, Zalavras and colleagues demonstrated that deficiencies in protein C and protein S, which lead to thrombophilia, have been associated with OFH. Jones LC et al. studied blood samples from 45 patients with OFH, five of whom had no known pre-existing conditions that could contribute to the disease. Compared to 40 age-matched healthy controls, patients with OFH were three times more likely to have a

genetic abnormality that promotes coagulation, regardless of the presence of comorbidities[66].

OFH has been observed more frequently in human immunodeficiency virus (HIV) patients, both with and without antiretroviral treatment. However, the role of antiretroviral therapy in the development of OFH remains controversial. It is unclear whether the association is solely due to protease inhibitors or if it involves a multifactorial link, including other risk factors such as the HIV infection itself, a history of systemic corticosteroid use, or hyperlipidemia [67-68].

Diagnostic Methods

The diagnosis of OFH is primarily based on imaging findings. However, taking a thorough medical history is crucial for screening potential risk and prognostic factors, determining if other joints are affected, identifying conditions that may present with similar symptoms, and guiding management. In many cases, predisposing factors and underlying conditions can be identified through the patient's history**.**

Radiographs are the most accessible screening tool for managing hip pain, owing to their low cost, simplicity, and widespread availability. In the case of OFH, the presence of a subchondral fracture, often referred to as the "crescent sign," indicates an advanced stage of the disease that is likely to progress to degenerative joint disease [70]. The crescent sign is best visualized on the frog-leg lateral view, as it provides a clear profile of the most common location for a subchondral fracture—the superior lateral portion of the femoral head's anterior segment.

Magnetic resonance imaging (MRI) is considered the imaging modality of choice due to its superior sensitivity and specificity when compared to plain radiographs, computed

tomography, or scintigraphy [71-73] . MRI is the most useful screening tool for early diagnosis, allowing for quantitative evaluation of the disease extent within the femoral head and accurate staging of the condition [71]. A single-density, thin "band-like" lesion with a low signal intensity rim surrounding the necrotic area on T1-weighted images, along with a "double-line" sign—characterized by a low signal intensity outer rim and a high signal intensity inner rim on T2-weighted images are considered diagnostic of the disease [72].

Computerized tomography (CT) is considered the most sensitive test for detecting subchondral fracture of the femoral head [76,77]. The orientation of the necrotic segment dictates the optimal imaging plane for visualizing the subchondral fracture. The most commonly affected necrotic zones are located in the anterior superior segment of the femoral head. A subchondral fracture is typically first identified along the superior lateral border of the femoral head. CT is also capable of detecting small areas of collapse that may not be visible on plain radiographs or Magnetic resonance imaging (MRI). However, despite these advantages, CT is less frequently used in the diagnostic process due to its ionizing radiation and the fact that MRI is essential for prognosis and treatment decision-making.

Technetium-99 isotope scanning shows the necrotic bone region as "cold" since it does not take up the radioactive isotope. In contrast, the surrounding rim of reactive bone remodeling appears "hot" on the scan. In the early stages of the disease, this results in a "cold within hot" pattern on the bone scan. Later, after a subchondral fracture occurs, the viable bone areas surrounding the necrosis engage in repair attempts and often appear as a "hot lesion," which can obscure the original cold area [75]. Although a bone scan is useful for detecting multifocal lesions, it has several limitations, including poor spatial resolution, low specificity in distinguishing between different disorders, and an inability to quantify the extent of the lesion [78]. For these reasons, nuclear studies are inferior screening tools in the management of OFH.

Prognosis

The prognosis based on radiological evaluation primarily depends on: (1) the presence or absence of femoral head collapse, (2) the extent of collapse, (3) the size of the necrotic lesion, and (4) any involvement of the acetabulum. Mechanical failure leads to the collapse of the femoral head. A crescent-shaped lucent lesion in the subchondral region indicates early collapse, while late collapse results in a change in the femoral head's contour. A contour change of more than 2 mm is associated with a worse prognosis. The extent of the necrotic area predicts the region of future collapse, making it a key outcome predictor, regardless of the treatment approach [79]. The combined necrotic angle of Kerboul [40] measured on radiograph or MRI [74] gives substantial detail on the size of the necrotic lesion, and are highly reliable and reproducible [80]. Similarly, some authors have suggested that the location of the necrotic lesion plays a role in treatment decisions, with small, medially

located lesions potentially being managed through observation alone[78]. Once arthritic changes are present in the acetabulum, treatments aimed at preserving the femoral head are likely to fail. [81].

Several classification systems have been developed to stage OFH, offering guidance on prognosis, decision-making, and potential outcomes. In a systematic review of the literature, Mont MA et al. [82] identified sixteen major classification systems used to classify and describe OFH. Among these, four classification systems accounted for more than 85.4% of the studies reported in the literature. The Ficat classification [83] was the most frequently used system (63%), followed by the University of Pennsylvania system (20%) [73,84] (Table 2), the Association Research Circulation Osseous (ARCO) system (12%) [85], and the Japanese Orthopaedic Association system (5%) [86,87]. In 1991, the Association Research Circulation Osseous (ARCO) classification system [88] was developed for clinical trials, by merging the Ficat, Steinberg, and Japanese Orthopaedic Association systems. Recently in 2019, the ARCO classification was revised [89] to provide uniform platform for clinical and research applications.

Treatment

The optimal treatment for OFH has been a topic of ongoing discussion and research for an extended period, yet no conclusive, evidence-based approach has been established. Treatment can generally be categorized into nonoperative and operative methods. The primary goal of treatment is to preserve the hip joint anatomy by preventing bone destruction and collapse of the femoral head. Conservative treatments, including pharmacological

agents, physical therapies such as hyperbaric oxygen and shockwave therapy, along with supportive measures to offload the hip, have been explored, but there is limited evidence supporting their widespread applicability. [90,93].

Non operative Treatment

Restricted weight-bearing to offload the affected hip has been recommended for patients awaiting surgery. A systematic review examining the natural history of untreated asymptomatic OFH found that 59% of such hips experienced disease progression over a mean period of seven years (range 0.2 to 20 years). The review also highlighted that the risk of collapse was highest in patients with sickle cell disease, while the lowest risk was observed in those with systemic lupus erythematosus. For large lesions (involving >50% of the femoral head), the chance of progression was 84%, compared to 32% for small- or medium-sized lesions [92].

Bisphosphonates

The primary action of bisphosphonates is to prevent osteoclastic resorption of bone tissue. The role of bisphosphonates in the treatment of OFH has been a subject of significant debate, with evidence from previous studies both supporting and opposing their use [93]. In a landmark clinicoradiological study, patients diagnosed with OFH were treated with alendronate for three years. Each patient received 10 mg of alendronate daily, along with standard precautions, and a daily oral supplement of 500 mg to 1000 mg of calcium and 400 IU to 800 IU of vitamin D3. Analgesics and non-steroidal anti-inflammatory drugs

(NSAIDs) were provided as needed for pain management. At follow-up visits conducted at eight and ten years, the authors found that alendronate had a significant role in preventing femoral head collapse, preserving joint function, and delaying the need for joint replacement surgeries when initiated in the early stages of the disease. However, evidence supporting its benefit when started in later stages of OFH remains limited [94,95]. In 2005, a randomized controlled trial found that patients who were treated with alendronate had a reduced risk of femoral head collapse and disease progression, provided that proper offloading of the affected hip was maintained[96].

In contrast to the studies mentioned above, several studies suggest that bisphosphonates have only a limited role in preventing disease progression. In a randomized controlled trial involving 32 patients, half of whom received alendronate and the other half a placebo, both groups showed similar rates of progression and femoral head collapse. Furthermore, THA was required in four patients from the bisphosphonate group and five patients from the placebo group [93]. Two meta-analyses, which included five eligible trials and a total of 329 patients, found that bisphosphonate therapy did not significantly reduce the progression to femoral head collapse. Additionally, there was notable heterogeneity between the trials, further complicating the interpretation of the results [97,98].

Agarwala et al. (99)(100) conducted a comprehensive study involving 395 hips, with an average follow-up of four years, which was later extended to 10 years for a subgroup of 40 patients (53 hips) with avascular necrosis (AVN) who received three years of oral alendronate treatment. The study found a significant reduction in pain and an improvement in function. Notably, the rates of radiologic progression and femoral head collapse were much lower than those reported in historical data for untreated AVN.

After 10 years, the study showed that 87% of hips (46 out of 53) had favorable clinical outcomes, with only 7% requiring hip replacement in Stage I, 5% in Stage II, and 26% in Stage III. Of the 34 hips in pre-collapse stages, 29% experienced collapse over the decade, with an average time to collapse of 4.2 years. Alendronate was particularly effective when initiated in the pre-collapse stages (Stage I or II), helping to slow disease progression and delay the need for hip replacement.

Lipid Lowering Agents (Statins)

An increase in the number and size of fat cells in the bone marrow predisposes individuals to osteonecrosis. Statins, by inhibiting adipogenesis, may play an important role in preventing osteonecrotic collapse. While they have a preventive role in steroid-induced OFH, statins may not be effective in reversing existing changes or promoting healing in such cases. [43, 101, 102]. A prospective study involving 2,881 renal transplant patients on corticosteroid therapy found that 338 patients were also receiving statins. The commonly used statins included lovastatin (20 mg), rosuvastatin, atorvastatin, and pravastatin, with dosages adjusted by physicians based on cholesterol levels. Among the 338 patients on statins, 15 (4.4%) developed OFH, compared to 180 of 2,543 (7%) patients who were not on statins [104].

Vasodilators

Prostacyclin analogs, such as iloprost, have been shown to reduce intraosseous hypertension and increase blood flow to ischemic areas. A prospective study evaluated the effects of iloprost on OFH in 95 patients, with the dosage titrated according to body weight. After an

average follow-up of three years, patients treated with iloprost demonstrated significant improvements in both pain and functional scores [103].

Anticoagulants

Vitamin K inhibitors, low-molecular weight heparins, and direct thrombin inhibitors have been used to prevent the progression of OFH in patients with coagulation disorders, such as thrombophilia. Limited data from a meta-analysis of four observational studies suggested that anticoagulants may be helpful in preventing the progression of primary OFH in patients without collapse. In particular, enoxaparin, administered at a dose of 6000 IU or 60 mg in a preloaded syringe daily for 12 weeks, was used in several studies, with positive results observed in preventing progression from the early stages of the disease[104]. Another study evaluating 60 patients with systemic lupus erythematosus who required high-dose glucocorticoid treatment found that warfarin therapy was associated with a reduced risk of developing OFH. In this study, warfarin was administered at doses ranging from 1-5 mg/kg/day (mean 2.9 mg). The control group did not receive warfarin. OFH developed in 19 of 58 hips (33%) in the control group, compared to 13 of 62 hips (21%) in the warfarin-treated group, suggesting a protective effect of warfarin against the development of OFH in this patient population[105]. There is a lack of multi-center studies and research exploring the effectiveness of various pharmacological agents compared to surgical methods in the treatment of OFH.

Biophysical Methods

Biophysical methods such as pulsed electromagnetic field therapy (PEFT), extracorporeal shock wave therapy (ESWT), and hyperbaric oxygen (HBO) have also been suggested for the treatment of OFH. PEFT is thought to work by stimulating osteogenesis and angiogenesis.

However, its effectiveness in the treatment of early-stage OFH has yet to be firmly established [106].

ESWT has been shown to restore tissue oxygenation, reduce edema, and induce angiogenesis. These effects suggest that ESWT could potentially serve as a feasible and effective alternative to more invasive surgical treatments for femoral head necrosis at various stages of the disease [107,108].

Hyperbaric oxygen (HBO) therapy increases the partial pressure of inhaled oxygen, which in turn boosts the production of reactive oxygen and nitrogen species in tissues. This process may stimulate the proliferation of endothelial progenitor cells, promoting neo-angiogenesis and neovascularization. HBO also raises extracellular oxygen concentration, reduces bone marrow pressure, and improves oxygen delivery to ischemic cells, thereby relieving compartment syndrome and helping prevent further necrosis[109-112]. A recent meta-analysis indicated that hyperbaric oxygen (HBO) therapy can provide favorable results, particularly in the early stages of OFH, with a notable positive response in the Asian population [109]. In a recent study involving 23 hips with stage II OFH, no statistically significant difference was observed between two groups treated with hyperbaric oxygen therapy and core decompression in terms of functional and radiological outcomes. This suggests that hyperbaric oxygen could be a viable noninvasive alternative to core decompression for managing early-stage OFH. [113].

Nonoperative modalities have generally proven ineffective in halting the progression of OFH and are not suitable for preventing collapse in the early stages of the disease. Since most

studies on nonoperative treatments come from single-center trials, are of low evidence, and yield inconclusive results, these approaches are typically recommended only as adjuncts to operative treatments [114].

Operative treatment

Operative options for OFH include procedures that aim to preserve the native hip joint, as well as total joint replacement when the joint cannot be salvaged. The choice of procedure depends on the extent, stage, and location of the disease. Joint-preserving procedures are designed to prevent or limit the progression of the disease and include core decompression and its variants (such as adjunctive grafting and stem cell therapy), bone grafting, and proximal femoral osteotomies. These procedures are typically recommended for symptomatic young patients who have not yet experienced femoral head collapse (pre-collapse) or for select patients with minimal collapse.

Core decompression

The necrotic process in OFH leads to cellular swelling and inflammatory cell infiltration, resulting in increased intraosseous pressure. Core decompression is a surgical procedure that involves drilling a core into the lesion to relieve this elevated pressure and create a channel for the formation of new blood vessels, promoting improved blood flow to the affected area [115]. Several studies have reported favorable outcomes with core decompression in symptomatic pre-collapse lesions, as well as in small lesions up to the early collapse stage of the disease. These procedures have been shown to help alleviate pain and slow disease

progression in patients with early-stage OFH [115-118]. Core decompression can be performed either using: (1) a single wide-bore trephine (10 mm), or (2) multiple small-diameter (3-8 mm) drillings.

In a study conducted by Etemadifar M et al. between 2010 and 2011 [119], patients who underwent core decompression surgery were monitored, and the results indicated a significant reduction in pain over time. Pain levels decreased from 6.82 ± 1.74 prior to surgery to 4.05 ± 1.29 at six months, and further dropped to 2.41 ± 1.82 at twelve months. The authors concluded that core decompression surgery effectively relieves joint pressure and pain, which may help slow disease progression and improve symptoms [119].

Rajagopal et al. [120] conducted a systematic literature review to evaluate the effectiveness of core decompression. After a minimum follow-up of two years, about 26% of the cases were eventually converted to total hip arthroplasty (THA). The review also found that patients with Ficat stage I disease and lesions affecting less than 50% of the femoral head were more likely to experience favorable outcomes, including no need for additional surgery and Harris Hip Scores greater than 70. These findings further support the idea that core decompression is most beneficial when performed in the early stages of the disease, leading to improved function and reduced pain.

A recent meta-analysis examining the outcomes of core decompression in 2,441 hips across 32 studies reported an overall success rate of 65% at an average follow-up of 54.3 months (range 2-228 months). This suggests that core decompression can be an effective treatment for a significant proportion of patients, particularly in the early stages of OFH [118]. A meta-analysis comparing 22 studies of core decompression with eight studies of nonoperative treatment showed a significantly higher success rate for stage I OFH hips treated with core

decompression, compared to those managed with conservative treatment alone. This highlights the effectiveness of core decompression in early-stage disease [121]. However, another review reported failure rates ranging from 14% to 25% in small lesions and 42% to 84% in larger lesions, suggesting that core decompression may be less effective as the size of the lesion increases [122]. A recent study from India reported a 75% survivorship rate following a mean follow-up of 53.5 months after isolated core decompression in 36 hips with stage I OFH. This suggests that core decompression can offer promising long-term outcomes in early-stage disease [123].

In 2004, Mont MA et al. described a core technique by drilling multiple times using a 3.2 mm pin [78]. In a study evaluating 120 hips treated with multiple drilling, Song WS et al. demonstrated a 78% survivorship rate at five years. Additionally, 88% of patients with small- to medium-sized lesions did not require further surgery at a mean follow-up of 7.2 years, indicating that multiple drilling can be an effective treatment for early-stage OFH in certain cases[121]. In 2013, Al Omran compared standard core decompression with multiple drilling and found no significant difference in the odds of improvement between the two procedures, with an odds ratio of 1.003 (p-value = 0.016). This suggests that both techniques may offer similar outcomes in terms of improving the condition of patients with OFH [125]. These studies suggest that multiple drilling can be an appropriate alternative to core decompression, offering similar benefits while potentially reducing the postoperative risk of femoral neck fractures. Additionally, arthroscopy-assisted core decompression provides the advantage of direct visualization of the articular cartilage, allowing for a better assessment of the degree of collapse. It also helps guide the reamer more precisely and minimizes the risk of joint penetration, offering a more controlled and refined approach to the procedure [126].

Stulberg et al. [127] conducted a randomized controlled trial (RCT) involving 55 hips, comparing the outcomes of core decompression to conservative treatment, using the Harris Hip Score (HHS). They found that core decompression was successful (i.e., it did not require total hip arthroplasty) in 70% of patients with Ficat Stage 1, 2, or 3, while conservative treatment had much lower success rates: 20% in Stage 1, 0% in Stage 2, and 10% in Stage 3. The authors concluded that core decompression is more effective than conservative therapy. These findings were further supported by Smith et al. [128], who reviewed 12 articles published between 1979 and 1991, with a mean follow-up of 38 months. In their analysis of 702 cases, they reported a success rate of 78% for Stage 1, 62% for Stage 2, and 41% for Stage 3 in patients treated with core decompression, compared to lower success rates for those receiving conservative treatment. Similarly, Mont et al. [129] analyzed 1,206 hips and found a success rate of 71% in Ficat Stages 1 and 2 for core decompression, compared to just 35% for conservative therapy**.**

Core Decompression with adjunctive therapy

Incorporating cell-based components into the tract created by trephine drilling is an adjunct to core decompression. Various adjuvants, such as tantalum rods, bone marrow stem cells, platelet-rich plasma (PRP), and other biologic materials, have been used with varying success rates. These adjuncts aim to enhance healing, promote tissue regeneration, and improve overall outcomes by stimulating bone repair and increasing blood supply to the affected area [130]. In 2016, Ma J et al. evaluated the efficacy of tantalum rods in 104 hips with ARCO grade II or III osteonecrosis and found that the survival rate was only 53% at a mean follow-up of 42.96 months (range 1-78 months). This suggests that while tantalum

rods may offer some benefit, their long-term effectiveness in more advanced stages of osteonecrosis may be limited [131].

Kang JS et al. compared the efficacy of core decompression alone with core decompression combined with bone marrow aspirate concentrate in 106 hips. At an average follow-up of 4.28 years (range 3-10 years), the cohort treated with bone marrow aspirate concentrate showed a significantly lower failure rate in the precollapse group (20% versus 50%, $p = 0.014$), a lower total hip arthroplasty (THA) conversion rate (28.3% versus 49%, $p = 0.028$), and a slightly lower rate of stage progression (35.8% versus 37.7%). These findings suggest that the addition of bone marrow aspirate concentrate may improve outcomes in the treatment of early-stage osteonecrosis of the femoral head [132]. In a prospective analysis of 35 hips that underwent core decompression combined with bone marrow aspirate concentrate and platelet-rich plasma, Houdek MT et al. reported promising results. At a mean follow-up of three years (range 2-4 years), 93% of the hips did not experience collapse, and 84% did not require total hip arthroplasty (THA). These findings suggest that the combination of bone marrow aspirate concentrate and platelet-rich plasma may be an effective adjunct to core decompression in preventing collapse and delaying the need for hip replacement in patients with osteonecrosis of the femoral head [133]. Similarly, other studies have also suggested that the augmentation of core decompression with bone marrow aspirate concentrate can decrease the conversion rate to total hip arthroplasty (THA) in pre-collapse osteonecrosis, but not in advanced lesions. A recent meta-analysis of fourteen randomized controlled trials compared core decompression alone with core decompression combined with autologous bone marrow stem cell therapy. The analysis found that cell-based therapy significantly reduced the need for THA ($p = 0.007$), improved postoperative Harris Hip Scores (HHS),

and effectively delayed femoral head collapse. These findings support the use of cell-based augmentation in early-stage osteonecrosis as a means to enhance the outcomes of core decompression and prevent or delay the progression to joint replacement[134]. In a systematic review of eleven studies (Level of evidence I to III), Piuzzi NS et al. analyzed the efficacy of core decompression combined with various adjunctive therapies compared to core decompression alone. The review included 380 hips treated with cell-based therapies and 245 hips treated with core decompression alone. They found that only 24.5% of hips in the cell-therapy group showed radiographic progression of disease, compared to 40% in the core decompression-only group. Additionally, out of the ten studies that reported failure rates, nine demonstrated a lower conversion rate to total hip arthroplasty (THA) in the cell-therapy group (16% versus 21%). These findings suggest that cell-based adjuncts to core decompression can significantly improve outcomes by reducing disease progression and the need for THA, particularly in pre-collapse stages of osteonecrosis[135].

In summary, while the results of cell-based therapies combined with core decompression are promising, several challenges remain. These include the lack of standardization in harvesting, processing, and transplant techniques, as well as uncertainty about the optimal quantity of cells required for definitive success. Additionally, concerns about the potency of mesenchymal stem cells in patients with osteonecrosis further complicate their widespread implementation. As a result, while these therapies show potential, further research and standardization are needed before they can become routine practice in the treatment of osteonecrosis[114].

Non-vascularized bone grafting

Non-vascularized bone grafting is recommended for use in symptomatic precollapse and early postcollapse lesions, particularly when the overlying articular cartilage remains relatively intact. The main objectives of bone grafting in these cases are to provide structural support, create a scaffold for bone remodeling, reduce intraosseous pressure, and remove necrotic bone. Mont MA et al. outlined three primary techniques for bone graft placement:1)Phemister technique: A cortical bone graft is inserted through a core tract drilled into the femoral neck and head 2)Trapdoor technique: A graft is placed through a "trapdoor" created in the articular cartilage of the femoral head 3)Light-bulb technique: The graft is placed through a window created in the femoral neck at the base of the femoral head. These techniques aim to address the underlying pathology of osteonecrosis while preserving the femoral head structure and function in the early stages of the disease. [78].

Non-vascularized fibula has been explored as a cortical strut graft for use in core decompression procedures. This technique involves placing a single or double fibular graft into the tract created by the core decompression. In a study by Lakshminarayana S et al., 36 stage I hips treated with core decompression alone were compared with 40 stage II hips treated with a non-vascularized fibular graft. The mean follow-up period was 53.5 months (range 44–63 months). The study found that 25% of the hips treated with core decompression alone and 30% of those treated with fibular grafting showed radiographic progression to a more advanced stage. The authors concluded that both core decompression and fibular grafting are similarly effective in managing early-stage AVN, with no significant difference

in the progression of the disease[123]. In a study involving the use of a cortical strut graft (either cortical tibial autograft or fibular allograft) following core decompression, 56% of 78 hips were able to avoid conversion to THA at a mean follow-up period of seven years. However, despite this survival rate, less than half of the study cohort showed significant clinical improvement. Additionally, 57% of the 44 hips that were not revised during the follow-up period exhibited an increase in their Ficat-Arlet stage, indicating disease progression. These findings suggest that while cortical strut grafting after core decompression can help delay THA, its long-term effectiveness in preventing disease progression and improving clinical outcomes remains limited [136]. Wu CT et al. conducted a study evaluating the use of double-fibular allograft strut grafts in 29 hips with femoral head collapse of less than 2 mm. The mean age of the patients was 38.9 years (range 24-58 years). The study reported impressive long-term results, with a five-year survival rate of 88.5% and a twelve-year survival rate of 76.9%. These findings suggest that double-fibular allograft strut grafting can be an effective technique for managing early-stage osteonecrosis of the femoral head, particularly in patients with minimal collapse [137].

After a mean follow-up of 52.6 months (range 24-80 months), Yildiz C et al. reported that 28.6% of 28 hips that underwent the light-bulb technique for core decompression and bone grafting showed radiographic progression of the disease. However, only 14.3% of the hips required conversion to total hip arthroplasty (THA). These results suggest that the light-bulb technique can be an effective joint-preserving procedure for early-stage osteonecrosis, with a relatively low rate of progression to THA [138]. These studies thus suggest that such bone grafting procedures are reserved for small to medium sized lesions in young adults.

Vascularized bone grafting

Vascularized bone grafting offers the added benefit of restoring blood supply to the necrotic femoral head, which is particularly advantageous in precollapse lesions. Among the different types of vascularized bone grafts, free vascularized fibular grafts and vascularized iliac crest bone grafts are commonly used. In a study by Ünal MB et al., 26 hips (17 with Ficat grade II and 9 with grade III) underwent free vascularized fibular grafting. At a mean follow-up of 7.6 years (range 5–9.2 years), the postoperative Harris Hip Scores (HHS) were reported to be >80 points in 15 of 16 hips with grade II disease and in 6 of 7 hips with grade III disease. This suggests that free vascularized fibular grafting can lead to significant functional improvement, particularly in patients with early-stage osteonecrosis [139]. Vascularized bone grafting, while promising for treating osteonecrosis of the femoral head, faces significant challenges that limit its widespread use. These include the need for a specialized surgical team, access to an operating microscope, and the technical complexity of the procedure. Additionally, long surgery times, concerns about graft viability due to potential issues with vessel anastomosis, and donor site morbidity (such as pain and functional limitations) make it a less attractive option for many surgeons. As a result, less invasive treatments like core decompression are often preferred, especially in settings where resources or expertise are limited[114].

Muscle-pedicled bone grafts utilize locally available bone while maintaining its vascular pedicle, in turn acting as vascularized bone graft. Meyer described quadratus femoris muscle-pedicle bone graft [140], while from Calcutta, Dr Baksi described sartorius-pedicle [141] and

tensor fascia lata muscle-pedicle iliac bone grafts [142]. Other muscle-pedicled bone grafts, such as the lateral femoral circumflex vessel-pedicled iliac graft and gluteus medius-pedicle greater trochanter flaps, have also been successfully used. In a randomized controlled trial by Li D et al., 47 hips with Ficat Stage I or II osteonecrosis were treated with either core decompression and cancellous bone grafting or quadratus femoris muscle-pedicle bone graft. At an average follow-up of 2.5 years, only five hips (two in the core decompression group and three in the muscle pedicle graft group) progressed to stage III, and none required total hip arthroplasty. Both groups showed significant improvement in HHS, though no significant difference was observed between the two treatment options ($p > 0.05$) [140]. Zhang L et al. compared two types of vascularized pedicle grafts—sartorius muscle-pedicle iliac graft and circumflex iliac deep bone graft—in 199 hips with ARCO Stage II osteonecrosis, with a mean patient age of 35 years. At an average follow-up of 31.22 months (range 12-48 months), no radiographic progression was observed in 87.5% of the sartorius muscle-pedicle group and 88.2% of the circumflex iliac deep bone graft group[142]. Zhao D et al. reviewed 2,179 hips treated with lateral femoral circumflex vessel iliac grafts, with a median follow-up of 12 years (range 5-25 years). They reported that 13.1% of Stage II hips and 25.6% of Stage III hips showed radiographic progression, while 1.34% of Stage II hips and 24.4% of Stage III hips eventually required conversion to THA. [143].

Femoral osteotomy

Proximal femoral osteotomies aim to shift the necrotic segment away from the weight-bearing region of the acetabulum. Two common types are (1) angular intertrochanteric and (2) transtrochanteric rotational osteotomies. While rotational osteotomies offer a greater degree of translation for the necrotic area, they are technically challenging and carry a higher risk of non-union. [78]. The success rates of femoral osteotomies for osteonecrosis of the femoral head have been reported to range between 70% and 93%, depending on factors such as the stage of the disease, the type of osteotomy performed, and the patient's overall health [146]

In a study of 53 hips with early collapse of the femoral head, Hamanishi M et al. found that intertrochanteric curved varus osteotomy resulted in a 98% hip survivorship, with only one hip requiring conversion to THA [147]. In a prognostic level II study involving 113 hips with Ficat stage II and III osteonecrosis, treated with anterior transtrochanteric rotational osteotomy, 24% of hips experienced secondary collapse, and 12% required conversion to THA after a mean follow-up of 51.3 months [148]. In a 2017 comparative study of 91 consecutive hips treated with transtrochanteric rotational osteotomy and 65 hips treated with transtrochanteric curved varus osteotomy, followed for at least five years, postoperative collapse occurred in 28.6% of the rotational osteotomy group and 10.8% of the varus osteotomy group ($p = 0.007$). Fifteen hips (16.5%) in the rotational osteotomy group and seven hips (10.8%) in the varus osteotomy group required conversion to THA. The survival rate, with radiographic collapse as the endpoint, was 68.7% for the rotational osteotomy group and 84.7% for the varus osteotomy group at nine years [149].

Femoral osteotomies can yield good results in the early stages of osteonecrosis, but their success diminishes once collapse has occurred. These procedures are less effective in post-collapse lesions, and their use for such cases has limited acceptance worldwide. Challenges include difficulty in selecting patients with lesions that are amenable to correction, technical complexities during the procedure, uncertain outcomes, prolonged immobilization required post-surgery, and complications when transitioning to THA if needed later [150].

Head sacrificing procedure

Joint-preserving procedures are often insufficient for treating large precollapse and postcollapse lesions of OFH. Once the femoral head collapses by more than 2mm or when arthritic changes are present, hip arthroplasty becomes necessary.

It is also considered a salvage option when other treatments fail. Large femoral head lesions, regardless of collapse, and cases involving delamination of the articular cartilage despite subchondral collapse, further extend the indications for THA. In these advanced stages, head-sacrificing procedures include: (1) hemi-resurfacing, (2) hemiarthroplasty, and (3) total hip arthroplasty, which may be either cemented or cementless, depending on patient factors and surgeon preference.

Hemi-resurfacing was initially introduced as an alternative to THA for young patients with OFH, where THA was considered an unfavorable option due to concerns about longevity and bone preservation. Initially, these procedures were seen as a "time-buying" measure after the failure of joint-preserving surgeries, as they helped preserve bone stock and typically had lower dislocation rates. However, a 27-year follow-up study by Amstutz HC and Le Duff MJ revealed that the survivorship of hemi-resurfacing was 80% at five years, 63% at ten years, and 36% at fifteen years, demonstrating a moderate long-term success rate but with eventual failure in a significant portion of cases [151]. After hemi-resurfacing, the acetabular cartilage often struggles to tolerate the metal bearing surface, leading to complications. In total hip resurfacing, metal-on-metal interfaces can cause significant issues, such as adverse reactions to metal debris, wear, and metallosis, which can reduce the longevity of the implant. Additionally, these procedures are associated with decreased survivorship over time and a higher risk of periprosthetic fractures, particularly in younger, more active patients. These complications have raised concerns about the long-term efficacy and safety of resurfacing

procedures, especially in the context of osteonecrosis where the femoral head may already be compromised [90]. As a reason to which, resurfacing procedures are seldom done these days.

Hemiarthroplasty can be considered as a treatment option for osteonecrosis of the femoral head when the acetabular cartilage remains free from arthritic changes. A study by Chan and Shih in 2000 compared hemiarthroplasty to THA and found no significant difference in the rate of subsequent procedures over an average follow-up of 6.4 years (range 4-12 years). This suggests that hemiarthroplasty, while preserving more of the natural acetabulum, may have similar outcomes to THA in terms of the need for additional surgeries, particularly when there is no significant damage to the acetabular cartilage [152]. However, as the years progressed, complications following hemiarthroplasty began to emerge. Yamano K et al. reported significant issues in their study of 29 uncemented bipolar hemiarthroplasties, with 22 patients (76%) experiencing complications such as femoral loosening, acetabular protrusion, and osteolysis at a mean follow-up of twelve years. These findings highlight the long-term challenges associated with hemiarthroplasty, particularly in terms of joint stability and the potential for significant bony changes, which can ultimately lead to the need for revision surgeries. [153]. Similarly, Mont MA et al. reported high failure rates and polyethylene wear [75], hence leading to fallout of hemiarthroplasty as a treatment option in OFH.

Cemented and cementless options of THA have been extensively analyzed for OFH. Goffin et al. conducted a study evaluating cemented THA in 93 hips of OFH patients following kidney transplant. They reported an impressive survivorship rate of 99% at ten years, which decreased to 64% at twenty years of follow-up. This highlights the high initial success rate

of cemented THA in managing OFH, although long-term outcomes demonstrate a notable decline in survivorship, emphasizing the challenges faced in maintaining joint function over extended periods [154]. A 2011 systematic review reported aseptic loosening rates of 8-37% for cemented THA performed for OFH before the 1990s [155]. The failure of cement interdigitation and subsequent loading in patients with osteonecrosis may be due to defective cancellous bone, which compromises the stability and long-term success of cemented THA [156].

Recent studies show that cemented THA for osteonecrosis now demonstrates low wear rates and over 90% survivorship at follow-up periods exceeding ten years. This improvement is attributed to advances in implant surfaces, highly cross-linked polyethylene, and better sterilization and storage methods [90]. Despite concerns about bone ingrowth failure in cementless prostheses for osteonecrosis, a study by Kim SM et al. reported a 94% survivorship in 64 hips treated with cementless implants over an average follow-up of 16 years, with no cases of aseptic loosening. [157]

In non-traumatic osteonecrosis, where patients are typically younger, short-stem femoral components are preferred to preserve bone stock. A study by Kim YH and Park JW, analyzing 335 total hip arthroplasties with ultra-short proximal loading uncemented femoral components for Ficat and Arlet stage III or IV osteonecrosis, reported 99% survivorship for both the femoral and acetabular components after a mean follow-up of 14.7 years [158]. Min BW et al. evaluated the wear of highly cross-linked polyethylene liners in 85 total hip arthroplasties performed in younger patients (average age 42, range 25-49) with osteonecrosis. After a mean follow-up of 13.5 years (range 10-17.3), all hips exhibited wear rates below 0.10 mm/year, well below the threshold for osteolysis, suggesting minimal concern for polyethylene wear in this patient group. [159].

Recent studies have compared the outcomes of THA in non-traumatic OFH to those in isolated osteoarthritis (OA) of the hip. Both conditions show excellent long-term clinical outcomes, despite the fact that OFH typically affects a much younger population. This comparison underscores that THA can be highly successful in younger patients with OFH, yielding results similar to those in OA patients, who are typically older [156]. Hart A et al. compared 416 hips with OFH who underwent THA to 416 hips with isolated osteoarthritis (OA). At a mean follow-up of 10 years, they found no significant differences in clinical outcomes or complications between the two groups. The median HHS was 93 points for both groups, and the 15-year revision rate was 6.6% for the OFH group and 4.5% for the OA group ($p = 0.09$) [160]. In the light of these studies, the outcomes of THA have drastically shown improvement over the years in spite of the young population of OFH, mainly owing to improvements in prosthesis design and surgical techniques.

Approach to management

The treatment approach for osteonecrosis of the femoral head (OFH) is multifactorial, influenced by factors such as the degree of blood supply disruption to the femoral head, the disease stage and classification, the extent of necrosis, joint function, as well as the patient's age, occupation, and ability to adhere to rehabilitation following joint-preserving procedures. A recent study [161] evaluated treatment outcomes based on the JIC classification, including 390 bilateral and 115 unilateral cases. The distribution of JIC types was as follows: 21 type A, 34 type B, 173 type C1, and 277 type C2 hips. At the time of diagnosis, 47% (238 out of 505 hips) had already experienced femoral head collapse. Among the 212 precollapse hips, the collapse rates at two and five years were 0% for type A, 7.9% and 23.2% for type B, 23.2% and 36.6% for type C1, and 57.8% and 84.8% for type C2, respectively. The study concluded that type A ONFH typically does not require further treatment, whereas precollapse type C2 ONFH necessitates urgent joint-preserving surgery. The high collapse rate for type C2 emphasizes the critical need for early diagnosis and intervention, especially in asymptomatic patients with this stage of ONFH.

Mont MA et al., after a thorough review of classification, prognosis, and clinical outcomes, categorizes OFH into stages based on the extent of collapse: precollapse, early precollapse (head depression ≤2 mm), and late collapse (depression >2 mm or acetabular changes). [70]. Depending on the stage of collapse and the size of lesion, the authors suggest the following algorithm for guiding treatment options.

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AIMS AND OBJECTIVES

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AIMS AND OBJECTIVES

Aim of the study – To compare the clinical, radiological and patient-reported outcomes of core decompression with bisphosphonate versus bisphosphonate alone in patients with early osteonecrosis of the femoral head.

Objectives

- Primary objectives –

  1. To assess the clinical outcomes (HHS and VAS Score) in patients with early osteonecrosis of femur head managed by core decompression with bisphosphonate versus bisphosphonate alone at six months

  2. To assess the radiological outcomes (progression of disease and collapse of femur head) in patients with early osteonecrosis of femur head managed by core decompression with bisphosphonate versus bisphosphonate alone at six months

  3. To assess the patient-reported outcomes (HOOS score) in patients with early osteonecrosis of femur head managed by core decompression with bisphosphonate versus bisphosphonate alone at six months

  4.To compare the clinical, radiological and patient-reported outcomes between the two groups at six months using Ficat and Arlet classification.

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- Secondary objectives-

    1. To assess the number of patients where there is requirement of conversion to total hip replacement (THR) due to the progression of disease in the above two groups.

    2. To compare the progression of the disease in these patients based upon site and size of lesion using JIC classification, irrespective of treatment given

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MATERIALS AND METHODOLOGY

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MATERIALS AND METHODOLOGY

Study design: **C**omparative observational study

Sample size:

Taking Harris Hip Score (HHS) as the primary outcome measure, Minimum clinically important difference (MCID) as 10 [161] and standard deviation (S.D.) of 12.2 [161] with power of the study as 80% and confidence interval (C.I.) of 95%, the sample size attained was 24.

Assuming 10% as loss to followup, a total of 26 patients were taken in each group. In our study group A has 26 participants and group B has 30 patients.

Place of the study-Department of Orthopaedics, AIIMS Bhopal

Time period: Eighteen months from the time of receiving letter of approval.

Study Population: Patients presenting to department of Orthopaedics with complains of hip pain who meet the inclusion and exclusion criteria

Inclusion criteria:

- Patients with early osteonecrosis of femur head (ARCO grade I and II and IIIA)
- Patients between 18-60 years of age

Exclusion criteria:

- Patients who do not give consent to participate in study
- Patients with late osteonecrosis of femur head (ARCO grade IIIB and IV)
- Patients with bilateral osteonecrosis of femoral head where one hip had surgical

intervention.

- Patients suffering from other major disorder which significantly affect the outcome measures.
- Patients with post traumatic osteonecrosis of hip.

PATIENT SELECTION AND ASSESSMENT

All patients presenting to department of Orthopaedics with complains of hip pain were evaluated for osteonecrosis of femoral head. Detailed comprehensive history (including hip pain, drug history, past history, personal and family history as per proforma) was recorded. Focused history to assess risk factors of osteonecrosis of femoral head was taken like; history related to alcohol intake, steroid intake, smoking, immunocompromised state like HIV, organ transplantation, sickle cell anaemia, trauma, autoimmune disease like Systemic lupus erythematosus (SLE), Cushing disease, chronic pancreatitis, coagulopathy etc. Thorough clinical examination (including general physical examination and hip examination as per proforma) was done in all patients.

Radiological investigations was done including the standard pelvis with both hip and frog leg lateral x-ray in suspected case of osteonecrosis of hip. If early osteonecrosis was suspected on clinicoradiological grounds, patients was sent for MRI (1.5/3T) Final diagnosis of osteonecrosis of femoral head was based on clinical, radiological and MRI findings.

Grading of osteonecrosis of femoral head was done based on the X-ray and MRI using

Association Research Circulation Osseous (ARCO) classification and Ficat and Arlet classification. Size and site of the lesion was accessed based on Japanese investigation committee (JIC) criteria.

This was done by two orthopaedic surgeon and final ARCO, Ficat and Arlet staging and JCI grading was based on consensus. Non contrast computed tomography (NCCT) hip was done in limited patients if required.

ARCO classification (revised 2019) [162] used in the study is described below:

TABLE 1: Revised 2019 Association Research Circulation Osseus staging criteria

ARCO stage	Image findings	Description
1	X-ray normal MRI abnormal	A band lesion of low signal intensity around the necrotic area is seen on MRI. A cold spot is seen on bone scan. No changes are seen on plain radiographs.
2	X-ray abnormal MRI abnormal	Osteosclerosis, focal osteoporosis or cystic changes are seen in the femoral head on plain radiographs or CT scan. Still there is no evidence of subchondral fracture, fracture in the necrotic portion or flattening of the femoral head.
3	Subchondral fracture on X-ray or CT	Subchondral fracture, fracture in the necrotic portion and/or flattening of the femoral head is seen on plain radiography or CT scan.
3A (early)		Femoral head depression ≤ 2 mm
3B (late)		Femoral head depression >2 mm
4	X-ray osteoarthritis	Osteoarthritis of the hip joint with joint space narrowing, acetabular changes and destruction are seen on plain radiographs.

MRI: magnetic resonance image, CT: computed tomography

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The JIC classification comprises four types: A, B, C1, and C2. The classification is based on the central coronal section of the femoral head on a T1-weighted MRI. The extent of osteonecrotic lesions was classified into the four types listed below (i.e. types A, B, C1, and C2), based on their size and location on T1-weighted MRI or radiography (Fig1)[163][164]

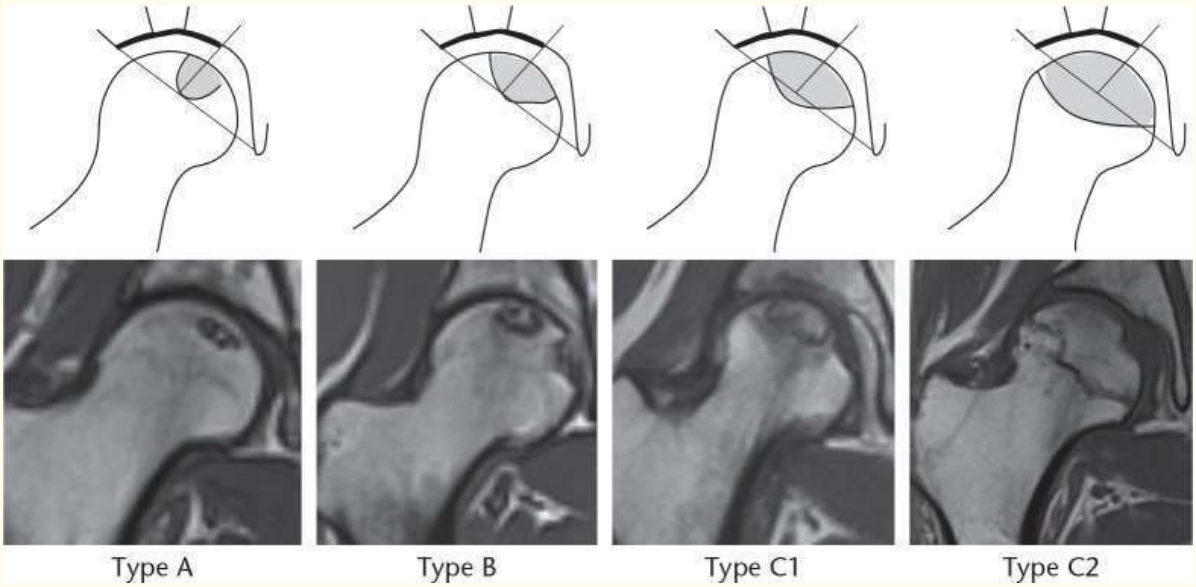

Figure 1 Japanese Investigation Committee (JIC) classification system

Schematic representation of T1-weighted MRIs of the 2001 revised Japanese Investigation Committee classification system[163][164] based on type. The classification scheme comprises four types (A, B, C1, and C2). Type A involves the smallest osteonecrotic lesions of the four types (present only in the medial one-third, or less, of the weight bearing surface). Type B involves osteonecrotic lesions present in the medial two-thirds, or less, of the weight bearing surface. Type C1 lesions are characterized by an osteonecrotic zone that spans more than the medial two-thirds of the weight bearing surface at the acetabular edge. Type C2 involves the large osteonecrotic zone that spans more than the medial two-thirds of the weight bearing surface and exceeds the acetabular edge.

All patients who fulfilled the inclusion and exclusion criteria and gave consent to participate in the study, were enrolled for the study. The severity of pain was recorded using Visual Analogue Score (VAS) score and clinical status was accessed using the harris hip score (HHS)[165]. Patient reported outcome was accessed using the Hip Disability and Osteoarthritis Outcome Score (HOOS) [165]

11-point numeric version of the Visual Analog Scale (VAS), also known as the Numeric Rating Scale (NRS) was used to assess the pain. It is a unidimensional tool for assessing pain intensity in adults [166-168]. Typically presented as a horizontal bar or line, the respondent chooses a number between 0 and 10 that best reflects their pain intensity. Here, 0 indicates no pain, while 10 represents the worst possible pain.[166-168]

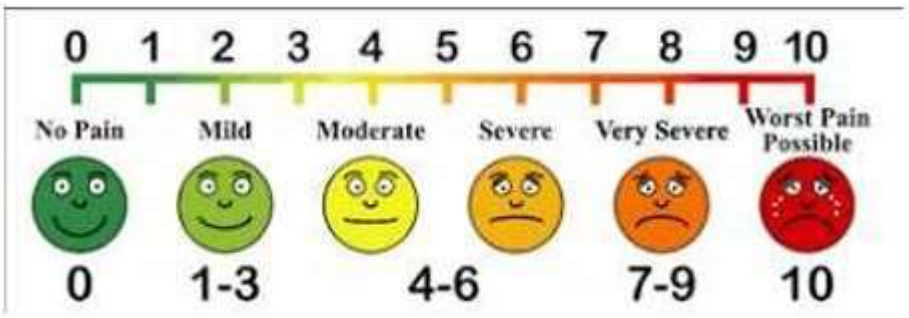

Figure 2 11-point numeric version of the Visual Analog Scale (VAS)

Harris Hip Score (HHS) [165] was used to assess hip function, a tool comprising ten items across four domains: pain, function, absence of deformity, and range of motion. The pain domain assesses

severity, its impact on activities, and medication needs. The function domain is divided into daily activities and gait. The deformity domain evaluates hip flexion, adduction, internal rotation, and leg length discrepancy, while the range of motion domain assesses hip mobility.[165] The HHS is structured into three sections: patient-reported questions about pain and its effects, followed by two sections where the care provider assesses hip joint and function. As a measure of hip dysfunction, higher scores indicate better outcomes, with a maximum score of 100[165]

Results can be interpreted as[120]: <70 = poor result; 70–80 = fair, 80–90 = good, and 90–100 = excellent. HHS questionnaires was filled on online website (https://www.orthopaedicscore.com/). (ANNEXURE II) Once the patient had completed the questionnaire, the result of it were downloaded and kept for further statistical analysis. In case person couldn't fill the questionnaire online, a trained person helped in filling the questionnaire.

The HOOS questionnaire was used to assess the severity of patient-reported outcomes. This self-administered tool takes about seven to ten minutes to complete and is designed to be straightforward and user-friendly. It contains 40 items, each with five response options ranging from 0 to 4 (0 indicating the worst possible score, 100 the best). Responses are provided using a standardized 5-point Likert scale, where options are scored as 0 (no), 1 (mild), 2 (moderate), 3 (severe), and 4 (extreme).The HOOS has five subcategories:

1. Pain (10 items with a total score of 40 points)
2. Symptoms and stiffness (five items with a total score of 20)
3. Activities of daily living (17 items with a total score of 68)
4. Function in sports and recreational activities (four items with a total score of 16)
5. Quality of life (four items with a total score of 16)

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HOOS questionnaires was filled on online website (https://www.orthopaedicscore.com/).(ANNEXURE III) Once the patient has completed the questionnaire, the result of it can be downloaded and was kept for further statistical analysis. In case person can't fill the questionnaire online, a trained person helped in filling the questionnaire.

All patient with ARCO grade I or grade II osteonecrosis of femoral head were be advised core decompression surgery. Patients who were willing for surgery underwent routine pre anesthetic checkup and standard core decompression (multiple small bore decompression) surgery along with bisphosphonate therapy (Group A). Patients who refuse surgical management were managed by bisphosphonate therapy alone (Group B). Patient were followed up on different time point that is day0, 2 weeks, 3 months and 6 months. VAS score was recorded at the different follow up time point that is at day 0, 2 weeks, 3 months and 6 months. Mean VAS score was then compared between the groups at all above mentioned follow up time point. Also HHS and HOOS score was recorded at the different follow up time point that is at day 0, 3 months and 6 months. Mean HHS and HOOS score were then compared between the groups at all above mentioned follow up time point.

Ficat and Arlet classification system was used to assess disease progression. 2 views of X-rays that is pelvis with both hip and frog leg lateral view were taken at day 0 and at 6 months and were compared in order to note any progression of disease by seeing any shift in the stage. Similarly JIC classification was used to assess the site and size of the lesion

preinterventionally at day 0.

Core decompression:

General anaesthesia or regional anaesthesia was given to the patient. Patient was placed in supine position on a standard table. The position of the femoral head was marked and the hip was prepared and draped. A Steinman pin or drill bit was inserted laterally and percutaneously under fluoroscopic guidance. The pin was advanced until it abuted the lateral cortex in the metaphyseal region opposite to the superior portion of the lesser trochanter. The femur was penetrated and the pin advanced through the femoral neck into the femoral head into the site of the lesion (as determined from preoperative x-ray or MRI assessment). Anteroposterior and lateral fluoroscopic views were taken while advancing the pin to ensure that it remained in the medullary canal of the femoral neck. Two to four drilling through lesions using one common entry point were done. Once the drilling was completed, the pin was removed and the wound closed using single nylon suture.

Postoperatively, patients were managed in the hospital till stable for discharge. X-ray were advised on post op day one. Proper wound care along with regular dressing was done during hospital stay. Antibiotics, supportive and symptomatic treatment was given.

Sutures were removed at postoperative day 14. Patient was allowed mobilization

with crutches from post op day two. After six weeks, the patients were allowed to mobilize without crutches. Postoperatively patient were taught about the hip abductor strengthening and ROM exercises.

Figure 3 Patient positioned supine and draping and painting done.

Figure 4 C ARM imaging done for assessing the location of hip joint

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Figure 5 Patient positioning on ot table and placement of guide wire before taking incision.

Figure 6 Confirming the placed drill bit under fluoroscopy

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Figure 7 Small skin incision taken on lateral aspect of proximal thigh for insertion of drill bit

Figure 8 Putting the guide wire with the help of power drill

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Figure 9 The femur was penetrated and the drill bit was advanced through the femoral neck into the femoral head into the site of the lesion

Figure 10 Anteroposterior and lateral fluoroscopic views were taken while advancing the drill bit to ensure that it remained in the medullary canal of the femoral neck. Two to four drilling through lesions using one common entry point were done.

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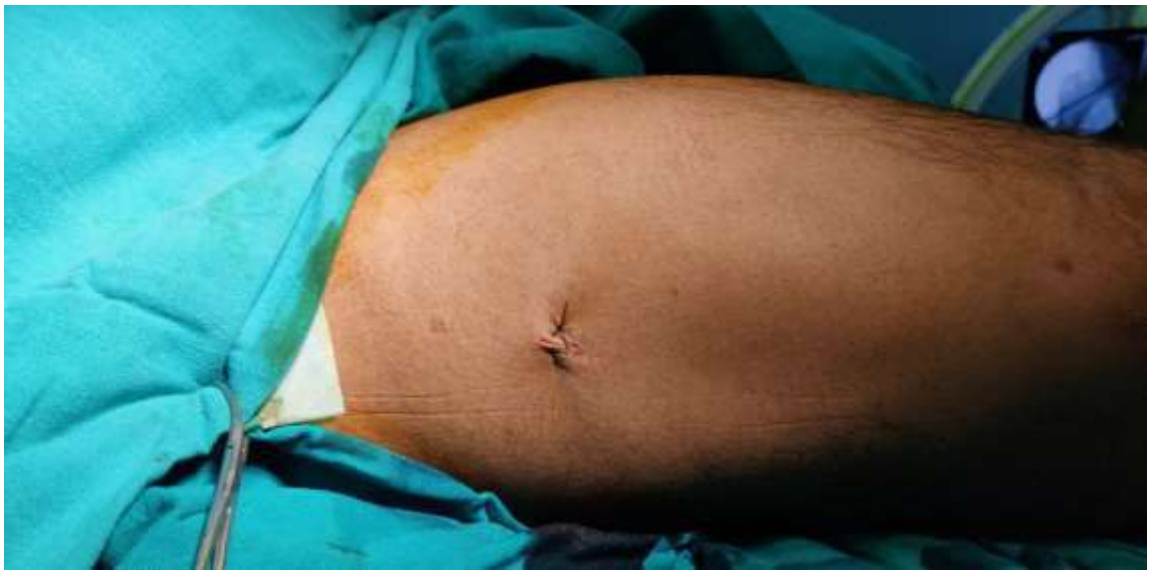

Figure 11 Closure of surgical site done

Bisphosphonate therapy:

Alendronate was given to the patient who were included in the study for both groups irrespective of the decision of agreeing for surgery or not. All the patients were treated with Alendronate 70 mg once a week, given early in the morning on an empty stomach with half a glass of water in sitting or standing position to avoid esophagitis. All patients received daily 500–1000 mg of calcium and 400–800 IU vitamin D3. Non-steroidal anti-inflammatory drugs (NSAIDs) and analgesics were permitted as needed.

Patients already being managed in the department, who fulfil the inclusion and exclusion criteria and whose records were available would also be included in the study.

Patients of the two groups were followed up at two weeks, six weeks, three months and six months for the first year and every six months thereafter. A detailed examination of patient was done. X-ray (standard pelvis with both hip and frog leg lateral) was done to access the progression of disease. NSAID/analgesic requirement side effects and complication were recorded, VAS score, HHS score and HOOS questionnaires were recorded on online performa (https://www.orthopaedicscore.com/).

The clinical, radiological and patient reported outcomes between the two groups were compared

The number of patients where THR was required was recorded.

The patients were divided into four groups based on the JIC criteria and the progression of the disease was accessed.

STATISTICAL ANALYSIS:

Descriptive statistics like frequency distribution, frequency, mean and standard deviation were used in the study. Statistics analysis was done using International Business Machines Corporation – Statistical Package for the Social Sciences (IBM-SPSS) version 22.

Descriptive analysis of the categorical variables was presented as percentage or proportion. Continuous variables were expressed as mean +/- SD (range). P-value < .05 were considered statistically significant. Parametric as well as non parametric statistical tests were used in order to compare the outcomes of two groups.

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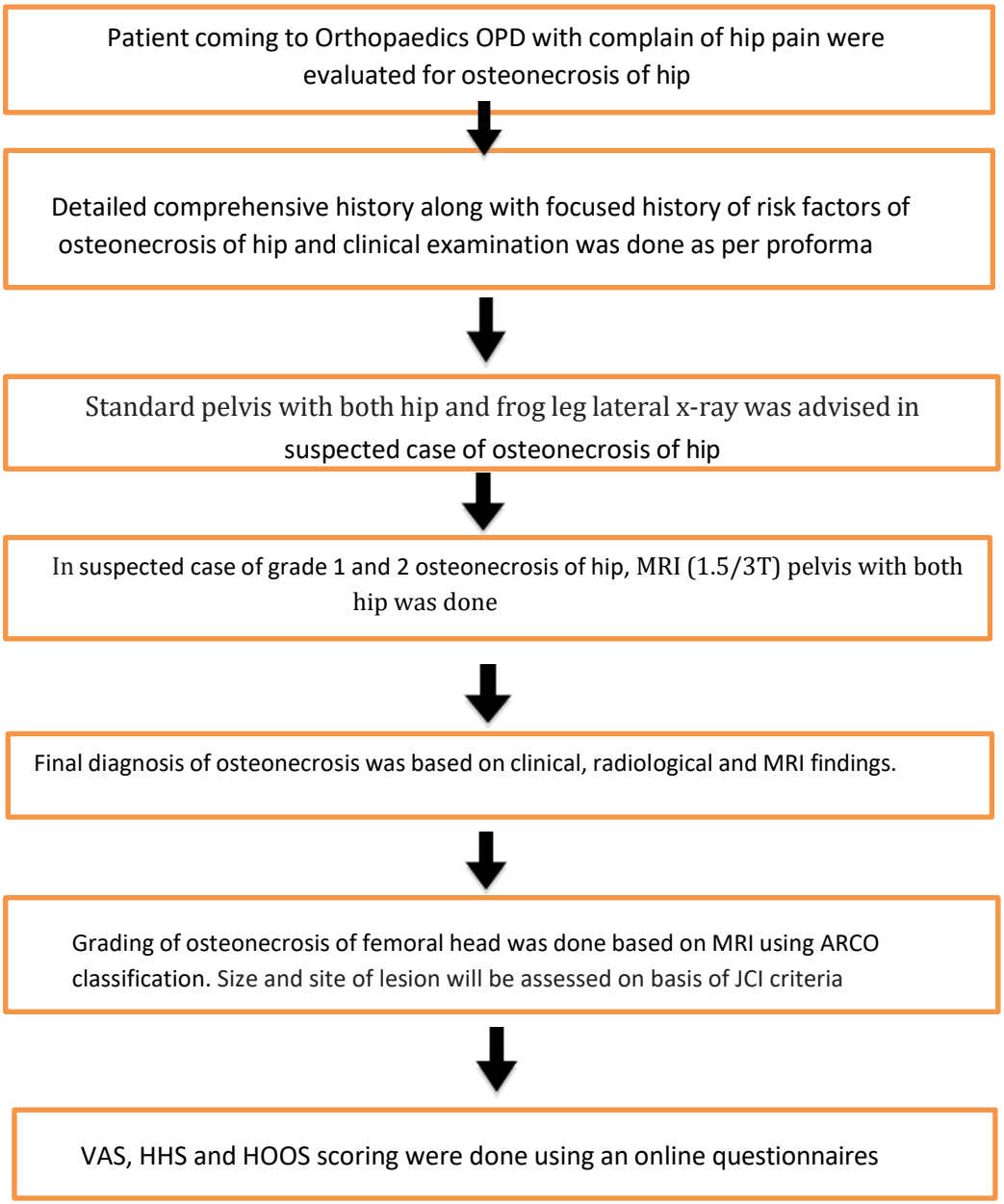
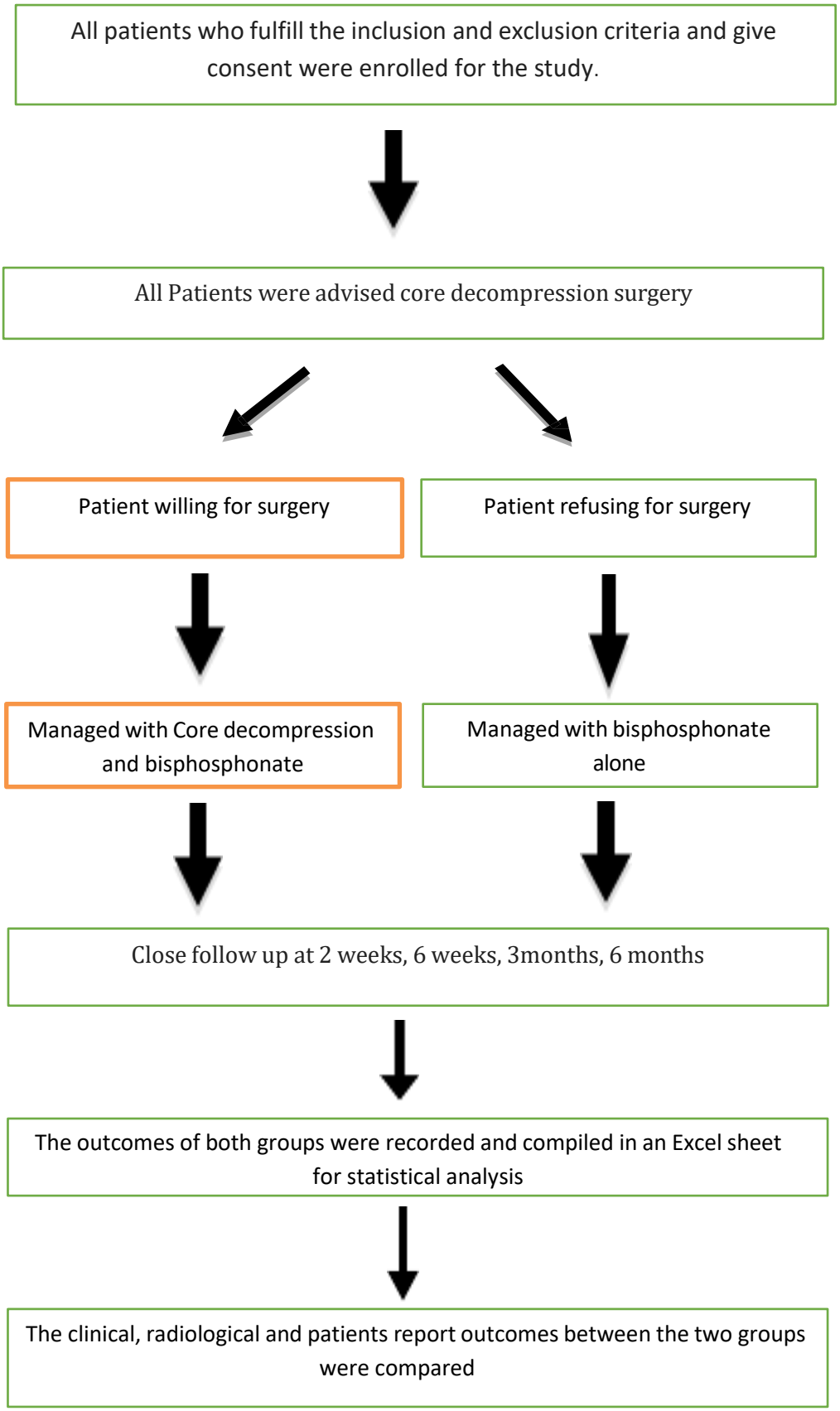
WORKFLOW


Patient coming to Orthopaedics OPD with complain of hip pain were evaluated for osteonecrosis of hip
Detailed comprehensive history along with focused history of risk factors of osteonecrosis of hip and clinical examination was done as per proforma
Standard pelvis with both hip and frog leg lateral x-ray was advised in suspected case of osteonecrosis of hip
In suspected case of grade 1 and 2 osteonecrosis of hip, MRI (1.5/3T) pelvis with both hip was done
Final diagnosis of osteonecrosis was based on clinical, radiological and MRI findings.
Grading of osteonecrosis of femoral head was done based on MRI using ARCO classification. Size and site of lesion will be assessed on basis of JCI criteria
VAS, HHS and HOOS scoring were done using an online questionnaires


All patients who fulfill the inclusion and exclusion criteria and give consent were enrolled for the study.
All Patients were advised core decompression surgery
Patient willing for surgery
Patient refusing for surgery
Managed with Core decompression and bisphosphonate
Managed with bisphosphonate alone
Close follow up at 2 weeks, 6 weeks, 3months, 6 months
The outcomes of both groups were recorded and compiled in an Excel sheet for statistical analysis
The clinical, radiological and patients report outcomes between the two groups were compared

OBSERVATION

OBSERVATION

Demographic data

The study included 56 participants with a total of 86 hips, divided into two groups: the CD + Alendronate (group A) and the Alendronate only (group B). The group A comprised 26 patients, accounting for 41 hips, with 9 females and 17 males, resulting in a gender distribution of 34.6% females and 65.4% males .The group B consisted of 30 patients, totaling 45 hips, with 5 females and 25 males, leading to a gender distribution of 16.67% females and 83.33% males. Overall, the study had 14 female patients (25%) and 42 male patients (75%), indicating a significant male predominance across both groups. However, this difference in gender distribution was not statistically significant (p = 0.122)

Table 2: Demographic characteristics of the patients

Demographic Characteristics		All (n = 56) mean ± SD (range)	Group A (n = 26) mean ± SD (range)	Group B (n = 30) mean ± SD (range)	p-value
Sex	Males	42	17(65.38%)	25 (83.33%)	0.122
	Females	14	9 (34.62%)	5 (16.67%)	
Age (in years)		34.286 ± 10.593 (18-60)	33.115 ± 10.144 (21-55)	35.300 ± 11.036 (18-60)	0.447

There were total of 56 individuals, with a mean age of 34.29 years (± 10.59, range: 18-60 years). When examining the two treatment groups, those receiving core decompression with alendronate (n = 26) had a mean age of 33.12 years (± 10.14, range: 21-55 years), while the group receiving alendronate only (n = 30) had a slightly higher mean age of 35.30 years (± 11.04, range: 18-60 years).

The age difference between the two groups was not statistically significant, as indicated by a p-value of 0.447.

Table 3: Data about number of hips involved

Intervention Group	Total Participants	Total Hips	Unilateral	Bilateral
Group A (n = 26)	26 (46.43%)	41 (47.67%)	11	15 x (2)
Group B (n = 30)	30 (53.57%)	45 (52.33%)	15	15 x (2)
Total	56	86	26	60

The study included two types of patients based on hip involvement: those with unilateral hip involvement and those with bilateral hip involvement. Patients with unilateral hip involvement presented with either Grade 1, Grade 2, or Grade 3a (early stage) osteonecrosis. In contrast, patients with bilateral hip involvement were further divided into two subcategories: the first group had both hips classified as either Grade 1, Grade 2, or Grade 3a (early stage) for which both hips were included in the study, while the second group featured one hip with Grade 1, Grade 2, or Grade 3a (early stage) which was included in the study and the other hip exhibiting Grade 3b or Grade 4 (late stage) was excluded from the study.

Table 4: VAS score in both groups

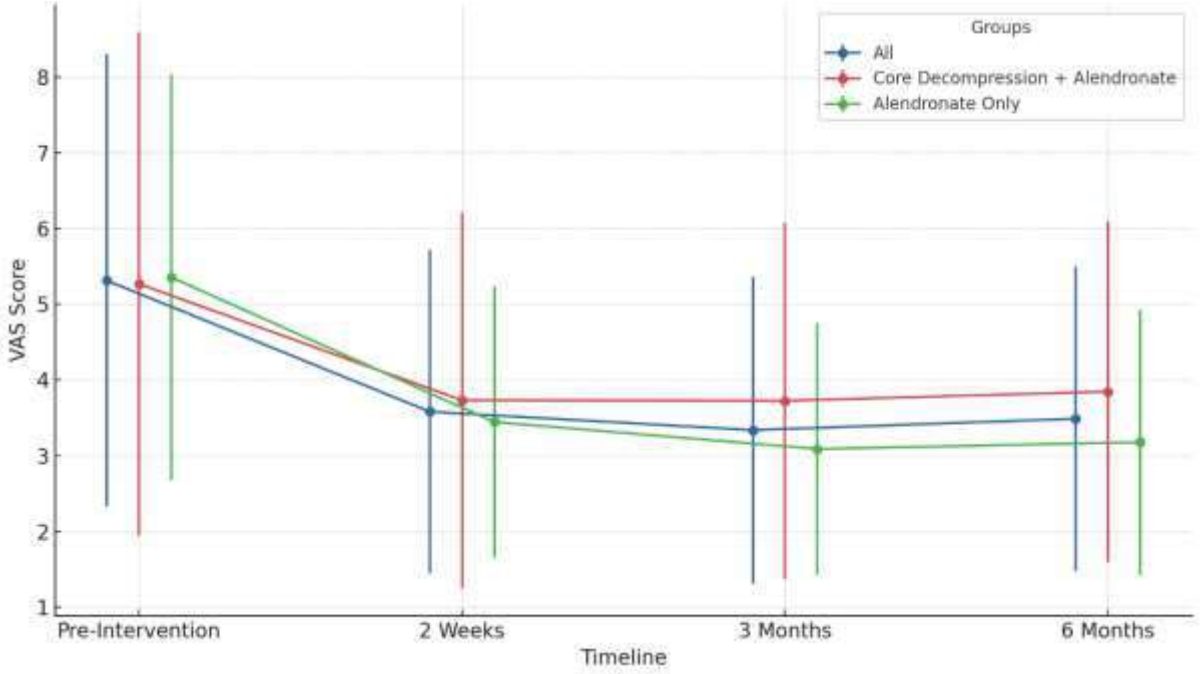
VAS score	All (n = 86) mean ± SD (range)	Group A (n = 41) mean ± SD (range)	Group B (n = 45) mean ± SD (range)	p-value
Pre-Intervention	5.314 ± 2.987 (0-10)	5.268 ± 3.324 (0-10)	5.356 ± 2.681 (0-10)	0.894
2 weeks post-Intervention	3.581 ± 2.139 (0-10)	3.732 ± 2.480 (0-10)	3.444 ± 1.791 (0-6)	0.543
3 months post-Intervention	3.338 ± 2.030 (0-9)	3.725 ± 2.353 (0-9)	3.089 ± 1.663 (0-6)	0.159

6 months post-Intervention	3.488 ± 2.015 (0-8)	3.846 ± 2.254 (0-8)	3.178 ± 1.749 (0-7)	0.138

The VAS scoring characteristics are summarized in the table, comparing pain levels across two treatment groups

Both treatment approaches resulted in a significant reduction in pain over the study period, but no statistically significant difference was observed between the Group A and Group B at any follow-up time point.

Figure 12- Descriptive plots for VAS



Plot showing reduction in VAS score at different follow up points in both groups

Table 5: Showing the differences of mean of VAS score for combined both groups (all hips) at different time points

Both Groups		Difference of means	p-value
VAS (pre-intervention)	VAS (2 weeks post-intervention)	-1.733	**<0.001**
	VAS (3 months post-intervention)	-1.976	**<0.001**
	VAS (6 months post-intervention)	-1.826	**<0.001**
VAS (2 weeks post-intervention)	VAS (3 months post-intervention)	-0.243	0.094
	VAS (6 months post-intervention)	-0.093	0.597
VAS (3 months post-intervention)	VAS (6 months post-intervention)	0.150	0.250

The differences in VAS scores between various time points in both groups are summarized in the table.

These results demonstrate that the intervention significantly reduces pain at 2 weeks, 3 months, and 6 months post-intervention compared to pre-intervention levels. Furthermore, there were no significant differences in pain scores among the post-intervention time points.

Table 6: Showing the differences of mean of VAS score for Group A at different time points

Group A		Difference of means	p-value
VAS (pre-intervention)	VAS (2 weeks post-intervention)	-1.536	**<0.001**
	VAS (3 months post-intervention)	-1.543	**<0.001**
	VAS (6 months post-intervention)	-1.422	**<0.001**
VAS (2 weeks post-intervention)	VAS (3 months post-intervention)	-0.007	0.531
	VAS (6 months post-intervention)	0.114	0.900
VAS (3 months post-intervention)	VAS (6 months post-intervention)	0.121	0.452

The differences in VAS scores between various time points in Group A are summarized in the table. These results demonstrate that the intervention significantly reduced pain at 2 weeks, 3 months, and 6 months post-intervention compared to pre-intervention levels. Additionally, there were no significant differences in pain scores among the post-intervention time points

Table 7: Showing the differences of mean of VAS score for Group B at different time points

Group B		Difference of means	p-value
VAS (pre-intervention)	VAS (2 weeks post-intervention)	-1.912	**<0.001**
	VAS (3 months post-intervention)	-2.267	**<0.001**
	VAS (6 months post-intervention)	-2.178	**<0.001**
VAS (2 weeks post-intervention)	VAS (3 months post-intervention)	-0.355	0.062
	VAS (6 months post-intervention)	-0.266	0.329
VAS (3 months post-intervention)	VAS (6 months post-intervention)	0.089	0.368

The differences in VAS scores between various time points in group B are summarized in the table. These results demonstrate that the intervention significantly reduces pain at 2 weeks, 3 months, and 6 months post-intervention compared to pre-intervention levels. Additionally, there were no significant differences in pain scores among the post-intervention time points.
While both groups showed significant pain reduction, there were no significant differences between them at any time point

Table 8: HHS score in both groups

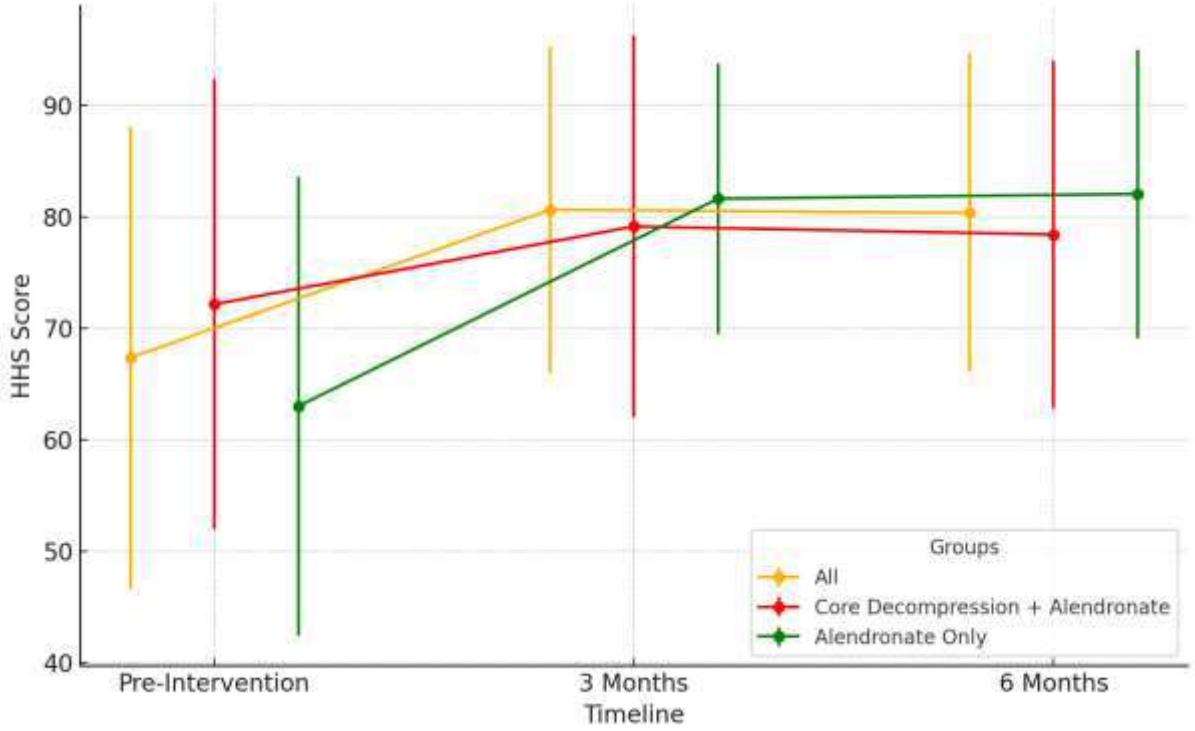
HHS score	All (n = 86) mean ± SD (range)	Group A (n = 41) mean ± SD (range)	Group B (n = 45) mean ± SD (range)	p-value
Pre-intervention	67.369 ± 20.788 (25-100)	72.159 ± 20.180 (34.8-100)	63.004 ± 20.586 (25-100)	**0.040**
3 months post-intervention	80.642 ± 14.661 (38.3- 100)	79.141 ± 17.121 (38.3-100)	81.636 ± 12.146 (60.8-100)	0.446
6 months post-intervention	80.364 ± 14.277 (42.3-100)	78.413 ± 15.603 (42.9-100)	82.056 ± 12.960 (42.3-100)	0.252

The HHS scoring characteristics are summarized in the table, comparing hip function levels across

two treatment groups

The HHS was significantly lower in group B as compared to group A indicating that the hip function was significantly poorer in group A compared to group B. However following the intervention in both groups the HHS improved at 3 and 6 months, it was noted that hip function improvement in group B were more and remain sustained at 3 and 6 months when compared to group A.

Figure 13 - Descriptives plots for HHS



Plot showing improvement in HHS score at different follow up points in both groups

Table 9: Showing the differences of mean of HHS score for both groups (all hips) at different time points

Both Groups		Difference of means	p-value
HHS (Pre-intervention)	HHS (3 months post-intervention)	13.246	**<0.001**
	HHS (6 months post-intervention)	12.995	**<0.001**
HHS (3 Months post-intervention)	HHS (6 months post-intervention)	-0.278	0.373

The differences in HHS scores between various time points in both groups are summarized in the table.

These results demonstrate that the intervention significantly improves hip function at both 3 months and 6 months post-intervention compared to pre-intervention levels. Furthermore, there were no significant differences in HHS scores among the post-intervention time points.

Table 10: Showing the differences of mean of HHS score for Group A at different time points

Group A		Difference of means	p-value
HHS (Pre-intervention)	HHS (3 months post-intervention)	6.982	**0.017**
	HHS (6 months post-intervention)	6.254	0.129
HHS (3 Months post-intervention)	HHS (6 months post-intervention)	-0.728	0.367

The differences in HHS scores between various time points in Group A are summarized in the table.

These results demonstrate that Group A significantly improves hip function at 3 months post-intervention compared to pre-intervention levels. Additionally, hip function improvement remains stable over time, although further improvement is not observed between 3 and 6 months.

Table 11: Showing the differences of mean of HHS score for Group B at different time points

Group B		Difference of means	p-value
HHS (Pre-intervention)	HHS (3 months post-intervention)	18.632	**<0.001**
	HHS (6 months post-intervention)	19.052	**<0.001**
HHS (3 Months post-intervention)	HHS (6 months post-intervention)	0.420	0.737

The differences in HHS scores between various time points for Group B are summarized in the table.

These results demonstrate that Group B significantly improves hip function at both 3 months and 6 months post-intervention compared to pre-intervention levels. Furthermore, there were no significant differences in HHS scores among the post-intervention time points, indicating that hip function improvement is effectively maintained over time without further significant change. However it should be noted that scores were significantly low in Group B when compared to scores of Group A which has high scores at baseline at day 0 .Therefore hip function improvement in Group B at 3 months and 6 months seems very large when compared to group A

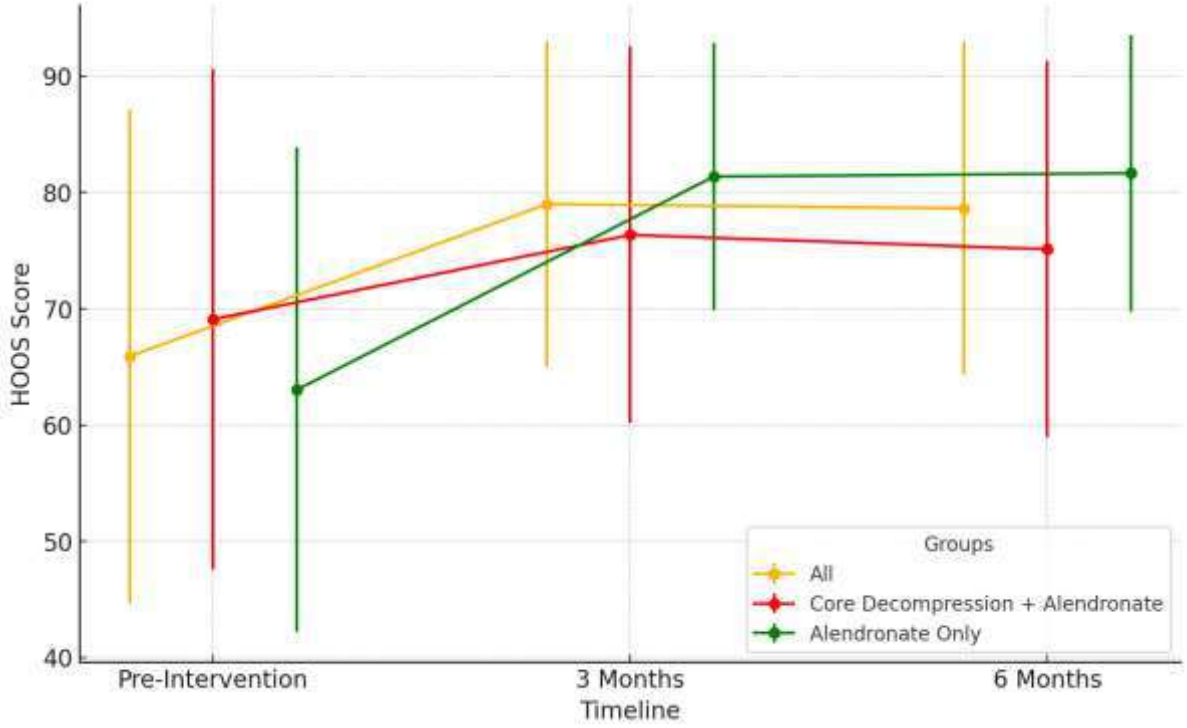
Table 12: HOOS score data in both groups

HOOS score	All (n = 86) mean ± SD (range)	Group A (n = 41) mean ± SD (range)	Group B (n = 45) mean ± SD (range)	p-value
Pre-intervention	65.918 ± 21.257 (18.1-100)	69.101 ± 21.510 (18.1-100)	63.018 ± 20.839 (35.5-100)	0.187
3 months post-intervention	79.005 ± 14.041 (38.8-100)	76.345 ± 16.200 (38.8-100)	81.369 ± 11.473 (55-100)	0.107
6 months post-intervention	78.625 ± 14.336 (31.9-100)	75.123 ± 16.194 (31.9-100)	81.660 ± 11.870 (41.9-100)	0.041

The HOOS scoring characteristics are summarized in the table, comparing hip function across two treatment groups

Both treatment approaches resulted in a significant improvement in hip function over the study period, with a statistically significant difference observed at six months favoring the Group B

Figure14- Descriptives plots for HOOS



Plot showing improvement in HOOS score at different follow up points in both groups

Table 13: Showing the differences of mean of HOOS score for both groups (all hips) at different time points

Both Groups		Difference of means	p-value
HOOS (Pre-intervention)	HOOS (3 months post-intervention)	13.087	**<0.001**
	HOOS (6 months post-intervention)	12.707	**<0.001**
HOOS (3 Months Post-intervention)	HOOS (6 months post-intervention)	-0.380	0.338

The differences in HOOS scores for both groups between various time points are summarized in the table.

The interventions significantly improved hip function at both 3 and 6 months compared to pre-intervention levels. Additionally, there were no significant changes between 3 and 6 months.

Table 14: Showing the differences of mean of HOOS score for Group A at different time points

Group A		Difference of means	p-value
HOOS (Pre-intervention)	HOOS (3 months post-intervention)	7.244	**<0.001**
	HOOS (6 months post-intervention)	6.022	**0.006**
HOOS (3 Months Post-intervention)	HOOS (6 months post-intervention)	-1.222	0.447

The differences in HOOS scores between various time points in group A are summarized in the table

Hip functions significantly improved in Group A at 3 months and 6 months.

Table 15: Showing the differences of mean of HOOS score for Group B at different time points

Group B		Difference of means	p-value
HOOS (Pre-intervention)	HOOS (3 months post-intervention)	18.351	**<0.001**
	HOOS (6 months post-intervention)	18.642	**<0.001**
HOOS (3 Months Post-intervention)	HOOS (6 months post-intervention)	0.291	0.527

The differences in HOOS scores for Group B between time points are summarized in the table.

There was significant and stable improvement in hip function from 3 to 6 months, with no further changes between these post-intervention time points.

Ficat & Arlet Grading to assess the progression of disease between treatment groups at 0 and 6 months

Table 16: Progression of disease in treatment groups

Intervention Group	Progression (Yes) (n = 22)	Progression (No) (n = 64)	P value
ALL (n= 86)	22(25.55%)	64	**<0.05**
Group A (n = 41)	17(41.46%)	24	
Group B (n = 45)	5(11.11%)	40	

Progression of disease in group A were significantly high when compared to group B.

Table 17: Progression of disease in **Ficat & Arlet** Grade 1 and 2

FICAT & ARLET Grading	Progression (Yes) (n = 22)	Progression (No) (n = 69)	P value
1 (n = 5)	3(60%)	2	**<0.05**
2 (n = 81)	19(23.4%)	62	

Progression of disease were significantly high in grade 1 when compared to grade 2

Table 18: **Ficat & Arlet** Grading of involved hip at 0 day and 6 months

Intervention Group	No. Of Hips	Stage	Preintervention	6 Months
ALL	86	1	5	2
		2	81	70
		3	0	14
Group A	41	1	3	0
		2	38	27
		3	0	14
GROUP B	45	1	2	2
		2	43	38
		3	0	5

For assessing disease progression by Ficat and Arlet staging over six months, we examined progression rates and specific stage changes in two treatment groups

Comparative Analysis Between Groups

The data reveal significant differences in disease progression rates between the two groups:

- Group A exhibited a higher progression rate (41.46%) compared to Group B (11.11%).
- Within the Group A, all Stage 1 hips advanced to higher stages, and 37% (14 out of 38) of the Stage 2 hips progressed to Stage 3.
- In contrast, Group B showed no progression among Stage 1 hips, and only 11.6% (5 out of 43) of the Stage 2 hips advanced to Stage 3.

TOTAL NUMBER OF THR DONE IN BOTH GROUP:

In our cohort, only two patients ultimately required total hip replacement, both of whom were in Group A

Table 19: JIC classification on the basis of site and size of the lesion among the treatment groups

JIC Grading	All (n = 86)	Core Decompression + Alendronate (n = 41)	Alendronate Only (n = 45)
A	25 (29.070%)	10 (24.390%)	15 (33.333%)
B	19 (22.093%)	10 (24.390%)	9 (20.000 %)
C1	22 (25.581%)	8 (19.512%)	14 (31.111%)
C2	20 (23.256%)	13 (31.707%)	7 (15.556%)

Table 20: Progression of disease among groups classified using JIC grading

JIC Grading	Progression (Yes) (n = 17)	Progression (No) (n = 69)
A (n = 25)	4 (16%)	21(84%)
B (n = 19)	2(10.5%)	17(89.5%)
C1 (n = 22)	6(27%)	16(73%)
C2 (n = 20)	5(25%)	15(75%)

JIC Grading and Disease Progression:

- **JIC Grade A**: Among the 25 patients in Grade A, 4 (16%) experienced progression, while 21 (84%) did not.
- **JIC Grade B**: Of the 19 patients in Grade B, 2 (10.5%) showed progression, while 17 (89.5%) did not. This grade demonstrates one of the lowest progression rates across all JIC grades.
- **JIC Grade C1**: Among the 22 patients classified as C1, 6 (27%) experienced progression, while 16 (73%) remained stable. The higher progression rate within this grade suggests that patients with more advanced initial disease may be at greater risk of worsening.
- **JIC Grade C2**: In this group, 5 out of 20 patients (25%) progressed, while 15 (75%) did not. Like Grade C1, C2 patients also demonstrate a relatively high progression rate.

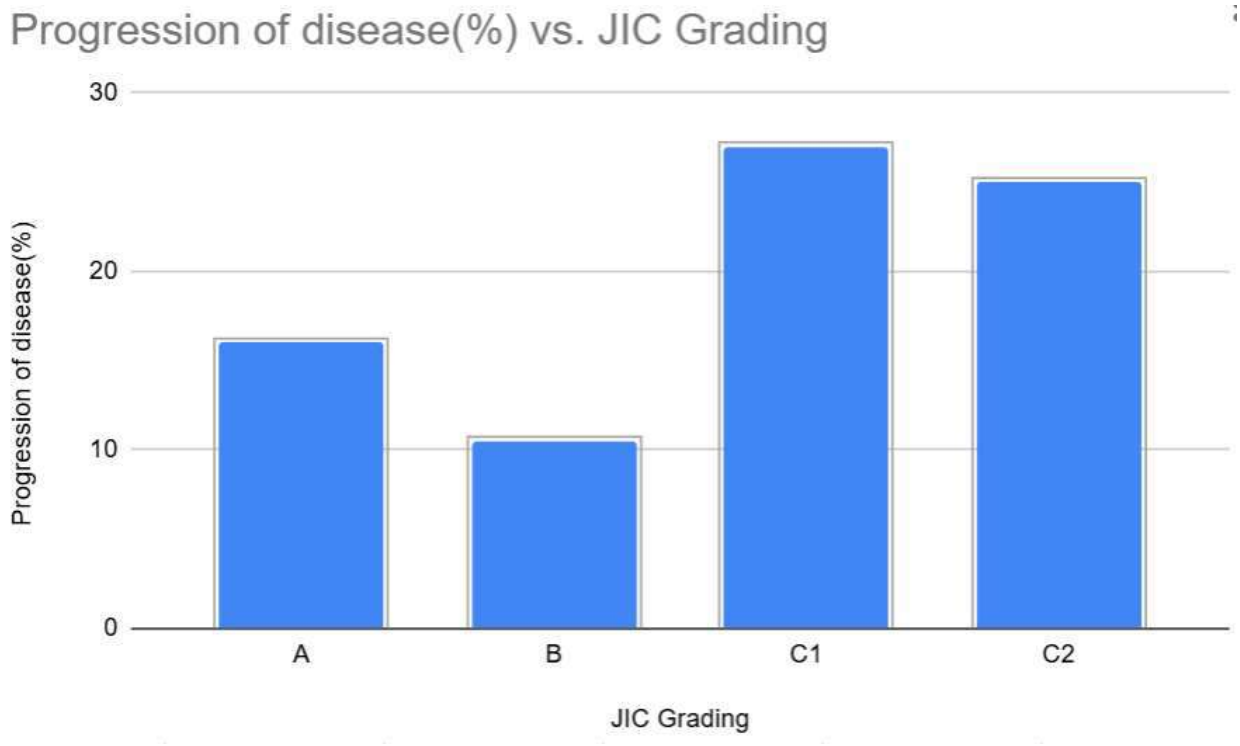


Figure 15 Bar chart showing Progression of disease among groups classified using JIC grading

There were no surgery related complication among the group A and also no side effect of alendronate drug noted among both treatment group during 6 months of study period.

Cases

Case 1 (Group A) 29y old female patient with osteonecrosis of bilateral femoral head

Ficat and Arlet grade 2 on both side on day 0 (preintervention).
Figure no.16 Case 1 preintevention xrays

Case 1(Group A) MRI **(ARCO grade 2 on both side)** preintervention

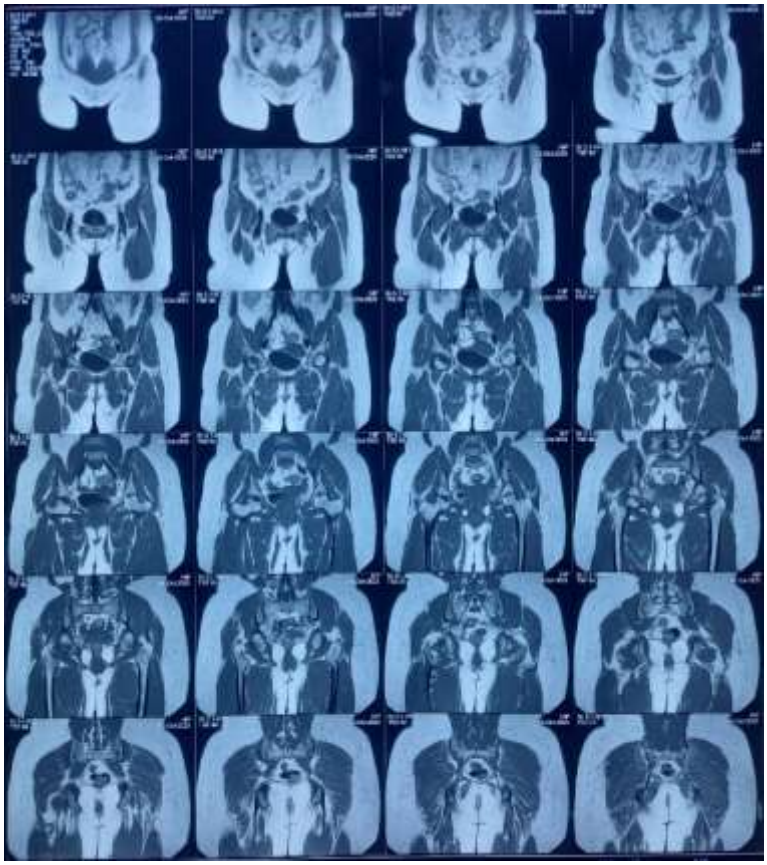


Figure no. 17 MRI of case 1

Ficat and Arlet grade 3 on right side and grade 2 on left side after 6 month post intervention (core decompression with alendronate)

Figure no.18 Case 1 six months postintevention xrays

Case 2 (Group A) 28y old female patient with osteonecrosis of bilateral femoral head

Ficat and Arlet grade 2 on both side on day zero (preintervention)
(figure no. 19 Case 2 preintervention xrays)
Case 2(group A) MRI **(ARCO grade 2 on both side)** preintervention

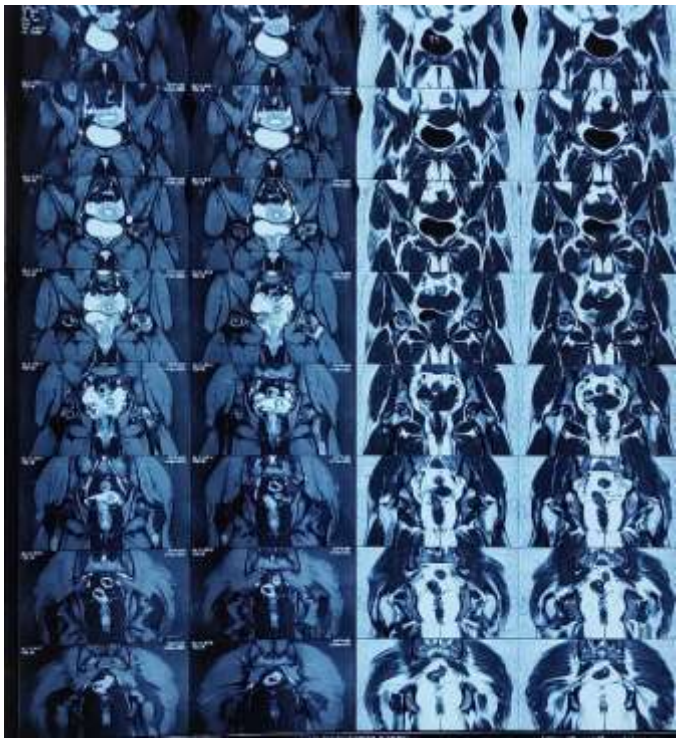
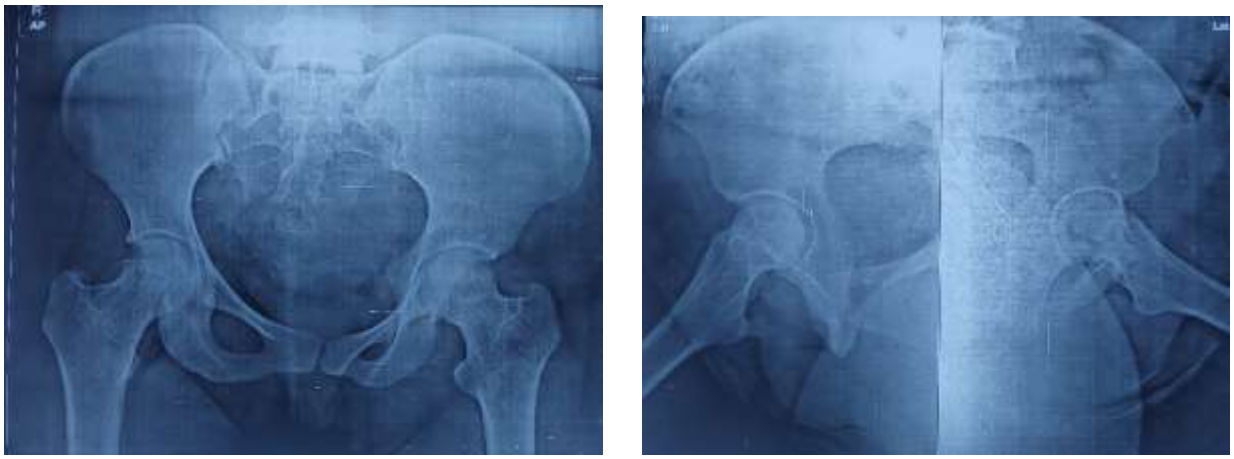


Figure 20 MRI of Case 2



Ficat and Arlet grade 2 on both side after six months post intervention (core decompression with alendronate)
(figure no. 21 Case 2 6 month posintervention xrays)

Case 3 (Group B) 21 y old male patient with osteonecrosis of bilateral femoral head

Ficat and Arlet grade 2 on right side on day zero (preintervention).
(figure no.22 Case 3 preintervention xrays)

Case 3(group B) MRI **(ARCO grade 2 on right side)** preintervention

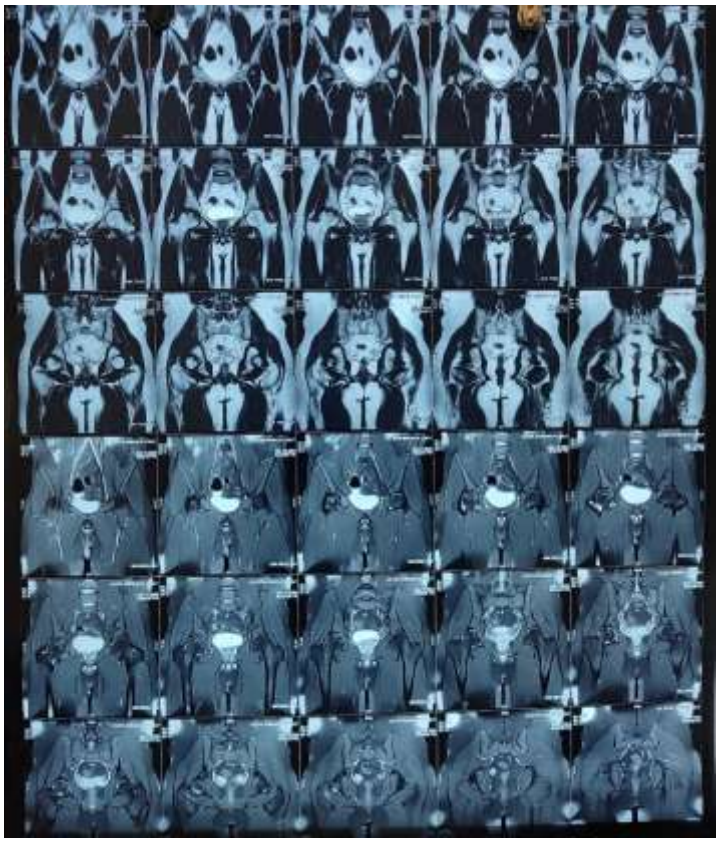
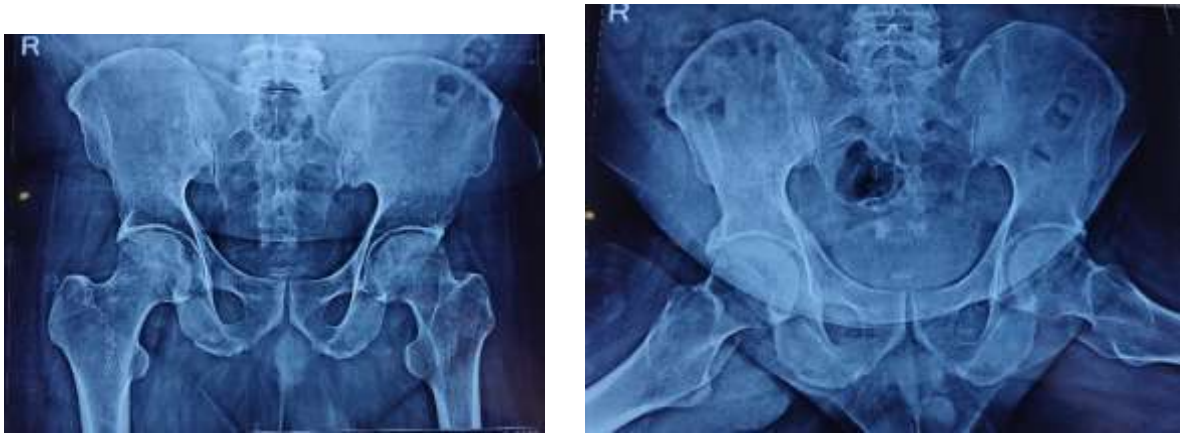


Figure 23 MRI of Case 3

Ficat and Arlet grade 2 on right side after six months post intervention (alendronate only)
Figure no.24 Case 3 six months posintervention xrays

Case 4 (Group B) 46y old male patient with osteonecrosis of bilateral femoral head



Ficat and Arlet grade 2 on both side on day zero (preintervention).
(figure no.25 Case 4 preintervention xrays)

Case 4(group B) MRI **(ARCO grade 2 on both side)** preintervention

Figure MRI of Case 4

Ficat and Arlet grade 2 on right side and 3 on left side after six months post intervention(alendronate only).

(figure no. 23 Case 4 six month posintervention xrays)

Case 5 (Group A) 46y old male patient with osteonecrosis of bilateral femoral head

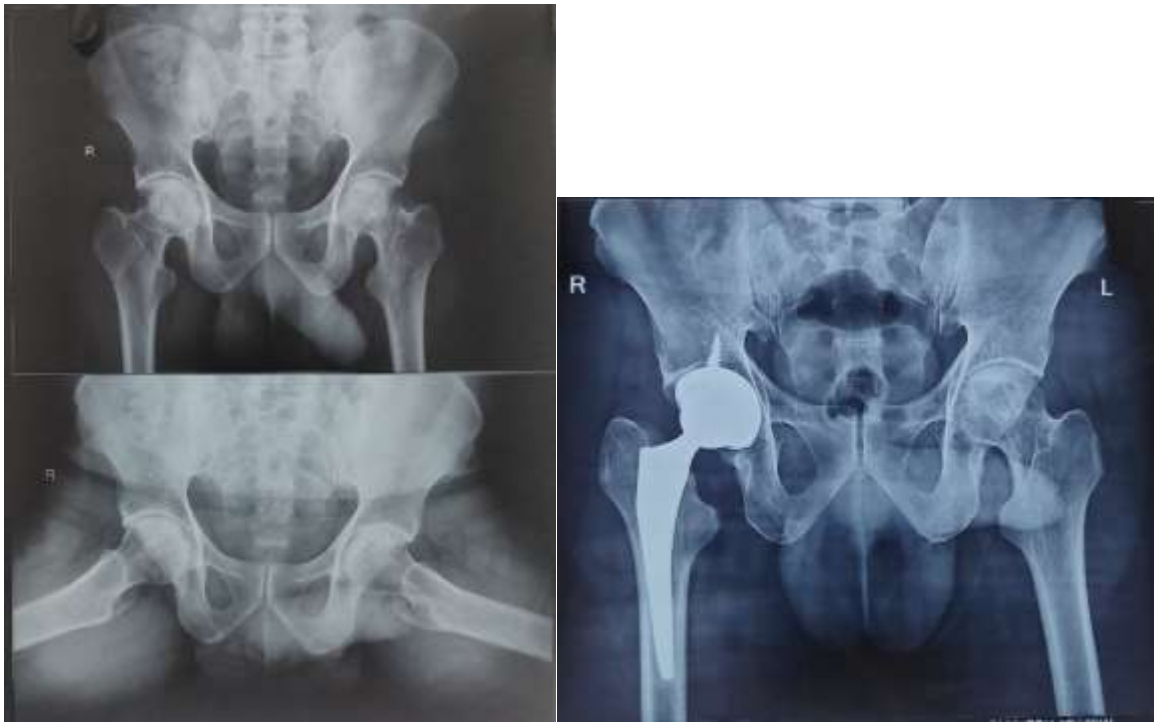


Figure no.24 Case 5 xrays

Ficat and Arlet grade 2 both side on day zero (preintervention) , bilateral core decompression was done and alendronate weekly dose given. After a time period of 3 months disease progressed on right side and patient got total hip replacement surgery done on right side.

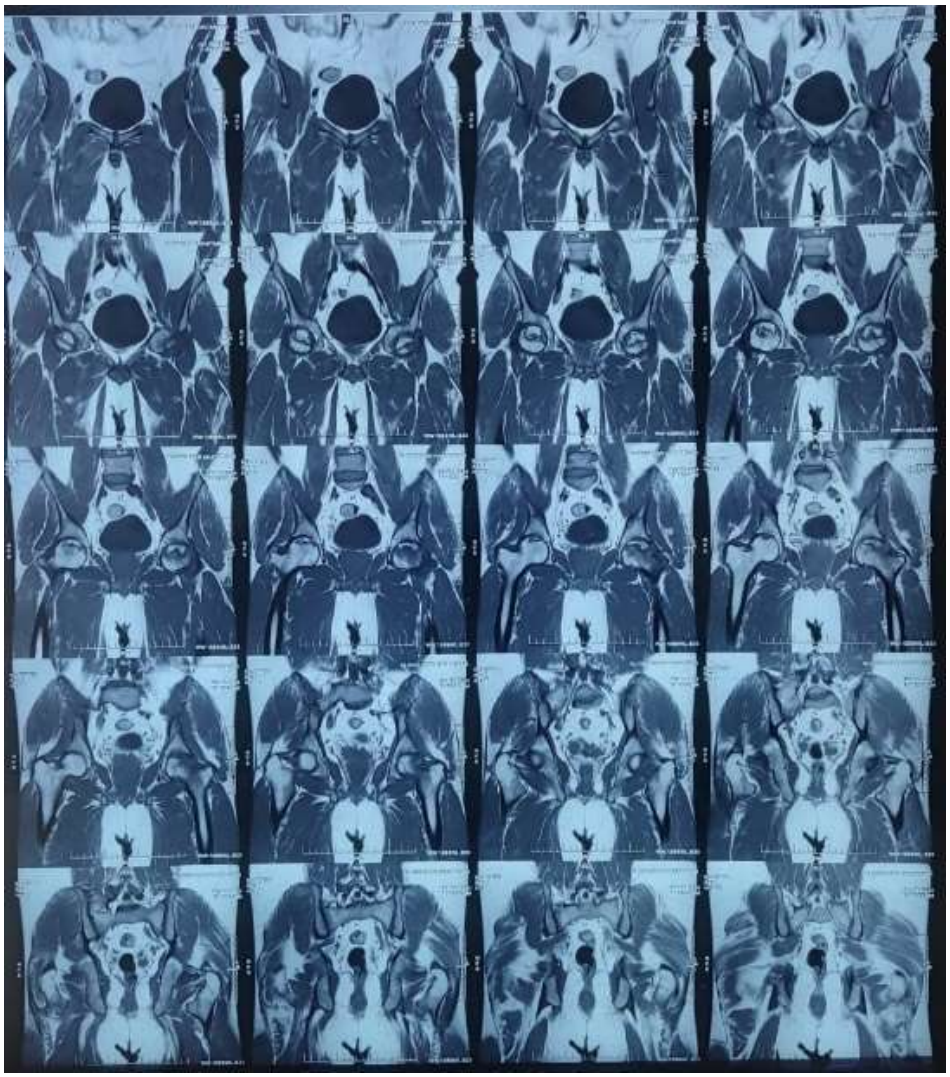


Figure MRI of Case 5 Group A (preintervention) ARCO grade 2 on both side

RESULT AND DISCUSSION

RESULT AND DISCUSSION

Our study aimed to compare the effectiveness of core decompression combined with bisphosphonate therapy versus bisphosphonate therapy alone in managing early-stage osteonecrosis of the femoral head. We evaluated several outcome measures, including pain reduction (VAS), hip function (HHS), patient-reported outcomes (HOOS), and disease progression (Ficat and Arlet classification). Many of the patients at our tertiary care institute who present with grade 1 or 2 osteonecrosis are already on some form of medical management, particularly bisphosphonates, and are offered core decompression as a surgical option. However, some patients refuse surgery, leading to the creation of two groups: one treated with core decompression and bisphosphonate therapy, and the other with bisphosphonate therapy alone. To the best of our knowledge, no previous studies have compared clinical, radiological, and patient-reported outcomes between these two treatment approaches, and our findings contribute to this ongoing debate about the best management strategies for osteonecrosis.

VAS score was used to assess the pain for both groups. VAS score was recorded at the different follow up time point that is at day zero, two weeks, three months and six months. Mean VAS score was then compared between the groups at all above mentioned follow up time point. Result of our study conclude that in terms of pain relief, both the core decompression with alendronate and alendronate-only groups showed significant reductions in VAS scores over time, with

improvements observed as early as two weeks after the intervention and maintained through three and six months. However, there were no significant differences in pain reduction between the two groups at any follow-up time point, suggesting that both treatment options are similarly effective in providing pain relief in the short term.

Harris Hip Score (HHS) was assessed for comparing hip function between the groups. HHS score was recorded at the different follow up time point that is at day zero, three months and six months. Mean HHS score was then compared between the groups at all above mentioned follow up time point. At day 0 that is preintervention the baseline scores were significantly low in alendronate groups when compared to scores of core decompression with alendronate group signifying that the baseline function parameter were lower in the alendronate only group as compared to core decompression with alendronate group. Both the groups were not comparable at day 0. Both treatment groups showed significant improvement compared to their pre-intervention scores at three and six months. However , there were no significant differences between the groups when mean of the HHS score were compared at three months and six months, indicating that both approaches were effective in improving hip function. However Alendronate only group showed a greater and more sustained functional improvement, while the core decompression with alendronate group exhibited a modest initial improvement that plateaued by six months.

Patient-reported outcomes was measured by the Hip Disability and Osteoarthritis Outcome Score (HOOS). HOOS score was recorded at the different follow up time point that is at day 0, three

months and six months. Mean HOOS score was then compared between the groups at all above mentioned follow up time point. Both groups demonstrated improvements in their scores at three and six months, but the alendronate only group showed significantly better outcomes at the six-month follow-up. However, there were no significant differences between the two treatment groups at the 3-month follow-up, suggesting comparable effectiveness in enhancing hip function in the short term for both interventions.

Ficat and Arlet classification system was used to assess the disease progression. 2 views of X-rays that is pelvis with both hip and frog leg lateral view were taken at day zero and at six months and were compared in order to note any progression of disease. We found that higher number of hip progressed from stage 1 to stage 2 or from stage 2 to stage 3 in the core decompression plus alendronate group when compared to the alendronate only group indicating that alendronate group was more effective in controlling the progression of the disease.

We found that the need for THR was low in both groups, with only two patients (3.6% of the cohort) requiring a hip replacement, and both were in the core decompression plus alendronate group.

JIC classification was used to classify the hip on the basis of site and size of the lesion for which MRI was done at day zero . X-rays were taken at day zero and at six months to compare the progression of disease on the basis of Ficat and Arlet classification between different individual

groups of hip which were previously classified under JIC criteria. We found that irrespective of the treatment given, patients who had higher JIC grading that is C1 and C2 progressed more as compared to the lower grade A and B.

In our study there were two groups that is core decompression with alendronate group and alendronate group. There are no studies that have compared these group. Hence we compared our results to study showing the effect of core decompression alone or alendronate alone on osteonecrosis of femoral head.

In our study we found that the pain and hip function improved in both groups. In a study done by Etemadifar M et al. during 2010-2011 [119] followed patients who underwent core decompression surgery, showing a significant reduction in pain severity over time. Pain levels decreased from 6.82 ± 1.74 before surgery to 4.05 ± 1.29 at six months, and further to 2.41 ± 1.82 at twelve months. The author concluded that core decompression surgery can effectively alleviate joint pressure and pain, potentially slowing disease progression and improving symptoms [119] supporting similar results seen in our study as VAS scores in our study also decreased in core decompression with alendronate group.

Rajagopal et al. [120] assessed the efficacy of core decompression in a systematic literature review. After a minimum 2-year follow-up, approximately 26 % of all cases were converted to THA. Furthermore, they found that those in Ficat stage I disease and lesions occupying <50 % of

the femoral head were more likely to achieve satisfactory outcomes (no additional surgery and Harris Hip Scores >70 points). The study further support the notion that core decompression is best when performed in the earliest stages of the disease and improves function and decreases pain.

Agarwala et al. [94-95] conducted an extensive study on 395 hips, with an average follow-up of four years, later extending the follow-up to 10 years for a subgroup of 40 patients (53 hips) with AVN. These patients received three years of oral alendronate treatment. This study shows that there was decrease in pain and improvement in the function. Importantly, rates of radiologic progression and femoral head collapse were significantly lower than historical data for untreated AVN. These findings were similar to our result supporting the fact that alendronate also help in decreasing the progression of disease.

In the above study conducted by Agarwala et al[94-95] after 10 years, 87% (46 of 53 hips) showed favorable clinical outcomes, with hip replacement required for only 7% in Stage I, 5% in Stage II, and 26% in Stage III. Among 34 hips in pre-collapse stages, 29% collapsed over a decade, with an average collapse time of 4.2 years. Alendronate proved especially effective when initiated in pre-collapse (Stage I or II) and also decreases the progression of disease as well as delaying the need for hip replacement. This findings align with result of our study that alendronates alone effective in controlling the progression of the disease.

In a study by Chen et al.[93], 83 patients with non-traumatic AVN of the femoral head received weekly oral alendronate (70 mg). Result of the study demonstrated significant improvements in pain and function scores for both ARCO I and ARCO II groups after three months. Notably, activity scores showed considerable improvement among ARCO II patients. The study concluded that alendronate is effective in treating early-stage non-traumatic AVN, with particularly strong effects observed in ARCO II patients. These findings support our results, showing that both treatments effectively reduce pain and improve hip function

Stulberg et al. [127](n = 55 hips) did an RCT comparing the results of core decompression with conservative treatment, using HHS. Core decompression was successful (didn't required total hip arthroplasty) in 70% in Ficat Stage 1, 2, or 3 whereas the results of the cases managed conservatively was only 20% successful in Ficat Stage 1, 0% in Stage 2, and 10% in Stage 3 and concluded that core decompression is more effective than conservative therapy. His results were also supported by Smith et al. [128](n = 702), in which he reviewed 12 articles published between 1979 and 1991 with mean follow up of 38 months and reported that cases treated with CD had 78% success in Stage 1, 62% in Stage 2, and 41% in Stage 3 in comparison with that of the cases treated with conservative therapy.

Similar results were also seen by Mont et al. [129] (n = 1206 hips) with 71% success rate in Ficat Stage 1 and 2 as compared to that of the conservative therapy with 35% success rate.

But contrary to the above study we found that core decompression with alendronate group, shows a higher rate of progression when compared to alendronate only group. This finding in our study resonates with the findings of study conducted by Smith et al.[169] (n = 114 hips) where 66.5% of failure was seen in Stage 2 and 100% failure in Stage 3. The author concluded that the poor results can be explained by the fact that, core decompression was done in higher stages like stage 2 and even in Stage 3 where the femoral head has already collapsed. Core decompression procedure delays the femoral head collapse and subsequent arthritis, but it does not completely stops the progression of the disease, as the length of follow up increases the number of failures also increases.[170]

We found that irrespective of the treatment given, patients who had higher JIC grading that is C1 and C2 progressed more as compared to the lower grade A and B. Yoon et al. found that after a mean follow up of 61 months, patients with Ficat stage II or III disease were more likely to require THA than those with stage I disease, especially when lesions were laterally or centrally located or occupied more than 30% of the femoral head [171] Lesion size also impacts outcomes, as shown by Mazieres et al., who found that smaller lesions (<23% of the femoral head) had lower rates of progression compared to larger lesions [172]

A recent study [173,174] assessing treatment outcomes based on JIC classification reported 390 bilateral and 115 unilateral cases. The JIC distribution included 21 type A, 34 type B, 173 type C1, and 277 type C2 hips. At diagnosis, 47.0% (238 of 505 hips) had already experienced collapse. For

the 212 precollapsed hips, the two- and five-year collapse rates were 0% for type A, 7.9% for type B, 23.2% and 36.6% for type C1, and 57.8% and 84.8% for type C2, respectively. The study concluded that type A ONFH generally does not require further treatment, while precollapse type C2 ONFH urgently calls for joint-preserving surgery. The high collapse rate highlights the importance of early diagnosis and intervention in asymptomatic patients with type C2 ONFH. This study aligns with our study that patients who had higher JIC grad that is C1 and C2 progressed more as compared to the lower grade A and B

Strengths of our study include its comparative design, which provides valuable insight into the effectiveness of core decompression combined with alendronate therapy versus alendronate therapy alone in managing early-stage osteonecrosis.

The study is done in a tertiary care institute replicating real world scenario where most of the patient coming to our OPD are already on alendronate and patient are offered core decompression as a surgical option. Hence making the results more applicable to everyday clinical practice and the findings are more likely to be generalizable to actual clinical settings.

By directly comparing these groups, the study offers practical evidence that can guide clinical decision-making where both non-surgical and surgical treatments are viable. The study also employs a comprehensive range of outcome measures including VAS , HHS , HOOS to capture a broad spectrum of patient outcomes, thus enhancing the robustness of the findings.

Limitation of our study includes short six-month follow-up period which may limit the understanding of long-term outcomes, as osteonecrosis progression can span years; thus, a longer follow-up would be necessary to fully assess the durability of pain relief, functional improvement, and disease stabilization.

Additionally, our study is not a randomised control trial therefore increases the risk of selection bias, potentially affecting the reliability of comparisons. Furthermore, the alendronate-only group served as a control, but the absence of a placebo group might limit interpretability.

Another limitation involves the use of HHS score, as patients with bilateral hip osteonecrosis may score lower due to higher stage in contralateral hip which may not be included in study and could inaccurately reflect their function. Also reliance on questionnaires for HOOS and HHS scoring may also introduce subjectivity and reporting bias.These limitations should be addressed in future studies to strengthen the reliability and generalizability of the findings.

SUMMARY

SUMMARY

Our study aimed to compare the clinical, radiological and patient reported outcomes of core decompression with bisphosphonate versus bisphosphonate alone in patients with early osteonecrosis of the femoral head in a tertiary care center, from January 2023 to April 2023. A total 56 patients (86 hips) were included in the study according to the inclusion and exclusion criteria.

Patients presenting with hip pain were initially evaluated through a comprehensive history, clinical examination, and radiological investigations, including **X-ray** and **MRI**, to diagnose osteonecrosis of the femoral head. The severity of osteonecrosis were graded using the **ARCO classification (2019)** and the **Ficat and Arlet staging system.** To assess treatment outcomes, following outcome measures were used: the **VAS** for pain intensity, the **HHS** for hip function, and **HOOS** questionnaire for patient-reported outcomes. Ficat and Arlet classification was used to assess the progression of disease. JIC classification was used to classify hips on the basis of site and size of the lesion.

All these patients were offered core decompression as a surgical option. However some of them refuse surgery leading to the creation of two groups: one treated with core decompression and bisphosphonate therapy, and the other with bisphosphonate therapy alone. Post-operatively, patients were mobilized with crutches and instructed in hip exercises for recovery. All patients,

regardless of surgical choice, received **alendronate 70 mg/week** along with calcium and vitamin D supplementation. Follow-up occurs at **2 weeks, 3 months,** and **6 months** to assess clinical, radiological, and patient-reported outcomes, with **X-ray** and **MRI** conducted to monitor disease progression and treatment efficacy.

We found that both core decompression with alendronate and alendronate alone group showed stastically significant reduction in pain in patients with early-stage osteonecrosis of the femoral head. Hip function showed stastically significant improved scores in both groups, although the alendronate-only group showed a more sustained improvement over time. Patient-reported outcomes via HOOS also showed stastically significant improvement, with the alendronate-only group achieving better functional scores at six months. Both treatment option reduces progression of osteonecrosis and progression of disease was less in the alendronate only group as compared to core decompression with alendronate group and hence delay the need for total hip replacement. It was also found that patients who had higher JIC grade progressed more as compared to the lower grade, irrespective of the treatment provided.

CONCLUSION

CONCLUSION

In this comparative observational study comparing core decompression with alendronate VS alendronate alone in treating early stage osteonecrosis of hip, we found that both the treatment are effective in reducing pain, improving function and delay progression of disease. However the improvement in the function is better in the alendronate alone group and is sustained beyond three months unlike core decompression with alendronate group where it plateaus at three months. The progression of disease as assessed by change in Ficat and Arlet grading was also more in the core decompression with alendronate as compared to alendronate alone group.

Hence we conclude that alendronate alone may be a better treatment options as compared to core decompression with alendronate in the short term, in patients with early osteonecrosis of femur head. Further studies with a larger sample size and long term follow-up are recommended to strengthen these findings and provide a clearer understanding of the long-term outcomes of these treatments.

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ANNEXURES

ANNEXURE 1

PROFORMA-Interview Data for Cases

- **Name:**
- **Age**
- **Sex**
- **Address/contact details**
- **Chief Complaints**
- **Family history**
- **Treatment history**
- **Risk factors** –steroid intake, blood transfusion, history of hospitalization, alcohol intake

- **GENERAL EXAMINATION:**
- **LOCAL EXAMINATION:**

✓ Gait
✓ Attitude
✓ Inspection
✓ Palpation
✓ Range of motion
✓ Measurements

- **INVESTIGATIONS:**

✓ Xray pelvis with both hip and frog leg lateral
✓ MRI bilateral hip
✓ NCCT bilateral hip

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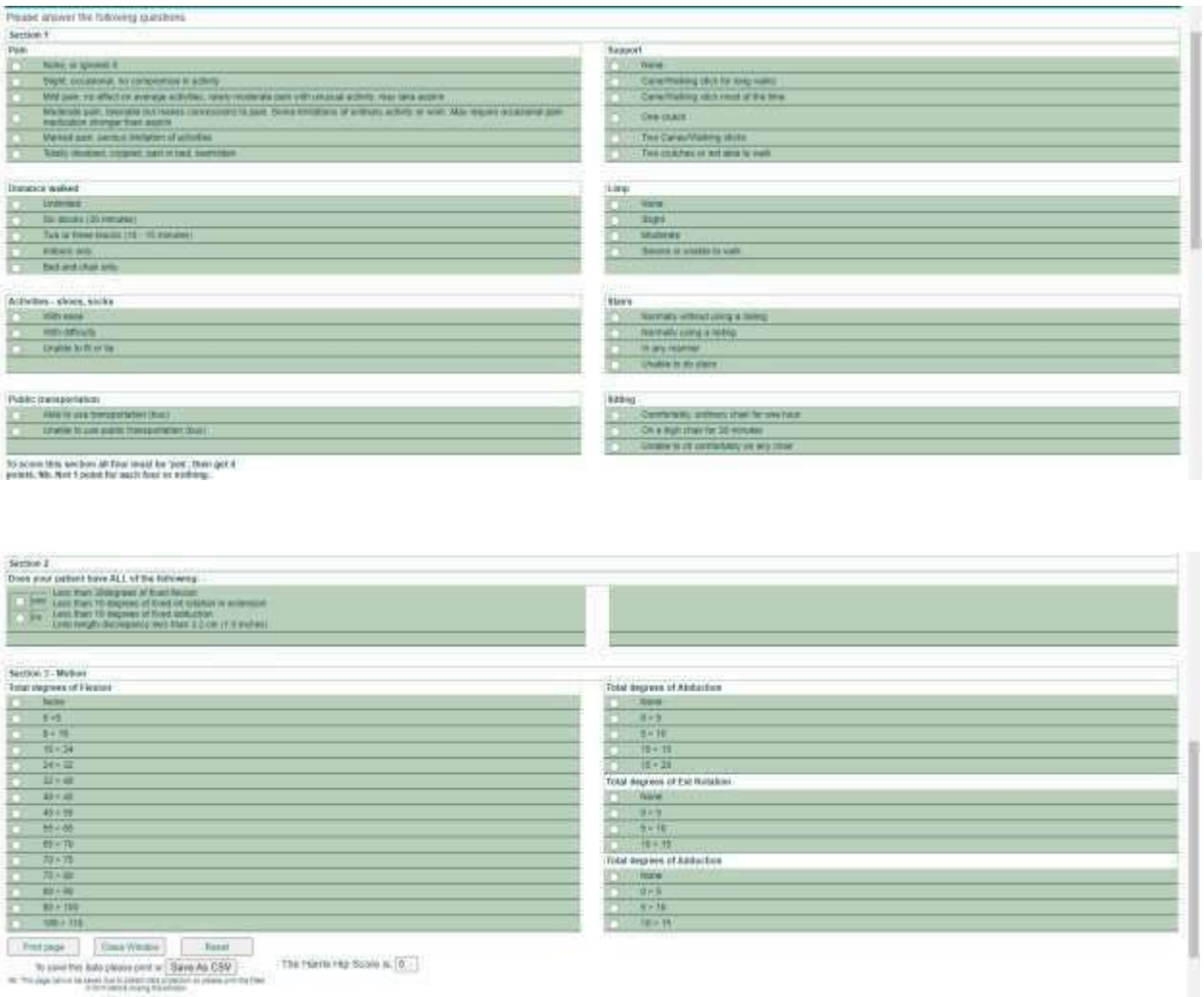
ANNEXURE II

HHS QUESTIONNAIRE ONLINE PROFORMA



Grading for the Harris Hip Score
Successful result
•post operative increase in Harris Hip Score of • 20 points • radiographically stable implant • no additional femoral reconstruction
Or
<70 Poor
70 - 79 Fair
80-89 Good
90 -100 Excellent
Reference for Score: Harris WH. Traumatic arthritis of the hip after dislocation and acetabular fractures: treatment by mold arthroplasty. An end-result study using a new method of result evaluation. J Bone Joint Surg Am. 1969 Jun;51(4):737-55. Link
Reference for grading: Marchetti P, Binazzi R, Vaccari V, Girolami M, Morici F, Impallomeni C, Commessatti M, Silvello L. Long-term results with cementless Fitek (or Fitmore) cups. J Arthroplasty. 2005 Sep;20(6):730-7.
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ANNEXURE III HOOS

QUESTIONNAIRE ONLINE PROFORMA

Hip disability and Osteoarthritis Outcome Score (HOOS)

Patient's name (or ref

Clinician's name (or ref)

Patient's d.o.b

INSTRUCTIONS: This survey asks for your view about your hip. This information will help us keep track of how you feel about your hip and how well you are able to do your usual activities.
Answer every question by ticking the appropriate box. If you are unsure about how to answer a question, please give the best answer you can.

Symptoms - These questions should be answered thinking of your hip symptoms during the **last week.**

S1. Do you feel grinding, hear clicking or any other type of noise from you hip?
Never | Rarely | Sometimes | Often | Always

S2. Difficulties spreading legs wide apart
None | Mild | Moderate | Severe | Extreme

S3. Difficulties to stride out when walking
None | Mild | Moderate | Severe | Extreme

Stiffness - The following questions concern the amount of joint stiffness you have experienced during the **last week** in your hip. Stiffness is a sensation of restriction or slowness in the ease with which you move your hip joint.

S4. How severe is your hip joint stiffness after first wakening in the morning?
None | Mild | Moderate | Severe | Extreme

S5. How severe is your hip stiffness after sitting, lying or resting **later in the day?**
None | Mild | Moderate | Severe | Extreme

Subtotal: 0

Pain

P1. How often is your hip painful?
Never | Monthly | Weekly | Daily | Always

What amount of hip pain have you experienced the **last week** during the following activities?

P2. Straightening your hip fully
None | Mild | Moderate | Severe | Extreme

P3. Bending your hip fully
None | Mild | Moderate | Severe | Extreme

P4. Walking on flat surface
None | Mild | Moderate | Severe | Extreme

P5. Going up or down stairs
None | Mild | Moderate | Severe | Extreme

P6. At night while in bed
None | Mild | Moderate | Severe | Extreme

P7. Sitting or lying
None | Mild | Moderate | Severe | Extreme

P8. Standing upright
None | Mild | Moderate | Severe | Extreme

P9. Walking on a hard surface (asphalt, concrete, etc)
None | Mild | Moderate | Severe | Extreme

P10. Walking on an uneven surface
None | Mild | Moderate | Severe | Extreme

Subtotal: 0

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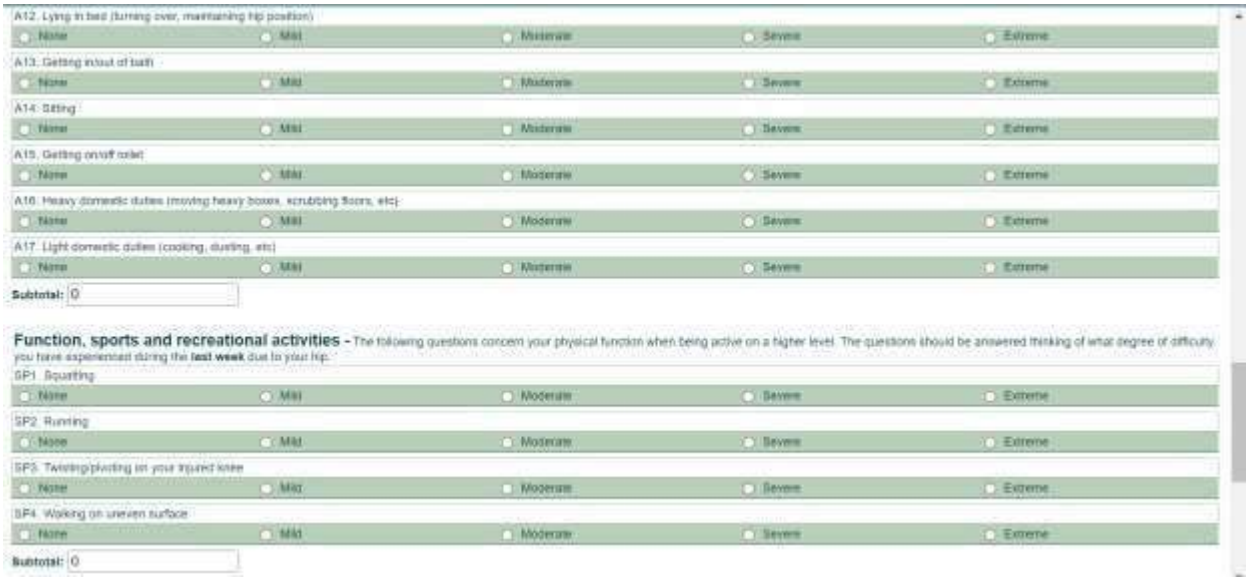
A12. Lying in bed (turning over, maintaining hip position)
None Mild Moderate Severe Extreme
A13. Getting in/out of bath
None Mild Moderate Severe Extreme
A14. Sitting
None Mild Moderate Severe Extreme
A15. Getting on/off toilet
None Mild Moderate Severe Extreme
A16. Heavy domestic duties (moving heavy boxes, scrubbing floors, etc)
None Mild Moderate Severe Extreme
A17. Light domestic duties (cooking, dusting, etc)
None Mild Moderate Severe Extreme
Subtotal: 0
Function, sports and recreational activities - The following questions concern your physical function when being active on a higher level. The questions should be answered thinking of what degree of difficulty you have experienced during the last week due to your hip.
SP1. Squatting
None Mild Moderate Severe Extreme
SP2. Running
None Mild Moderate Severe Extreme
SP3. Twisting/pivoting on your injured knee
None Mild Moderate Severe Extreme
SP4. Walking on uneven surface
None Mild Moderate Severe Extreme
Subtotal: 0

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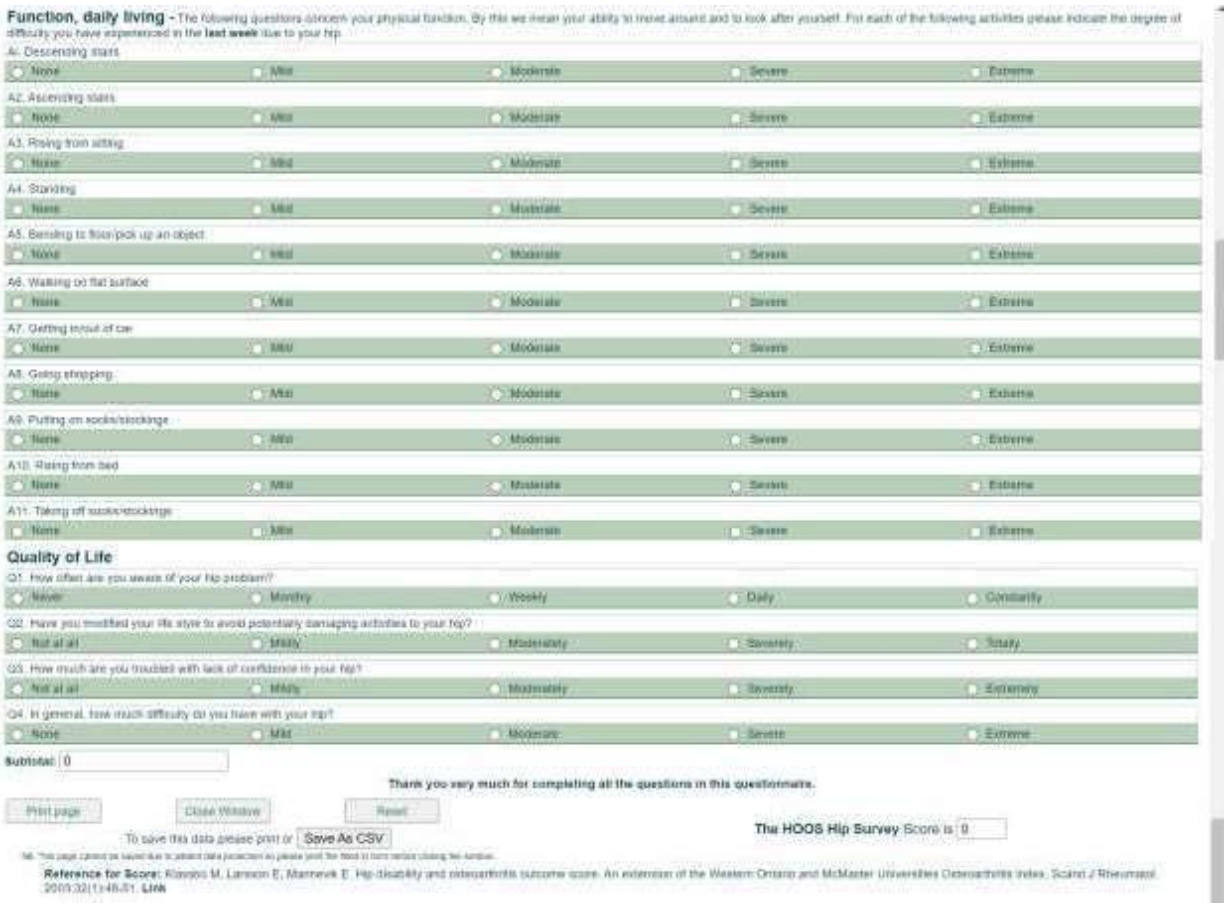

Function, daily living - The following questions concern your physical function. By this we mean your ability to move around and to look after yourself. For each of the following activities please indicate the degree of difficulty you have experienced in the **last week** due to your hip.

A1. Descending stairs
○ None ○ Mild ○ Moderate ○ Severe ○ Extreme

A2. Ascending stairs
○ None ○ Mild ○ Moderate ○ Severe ○ Extreme

A3. Rising from sitting
○ None ○ Mild ○ Moderate ○ Severe ○ Extreme

A4. Standing
○ None ○ Mild ○ Moderate ○ Severe ○ Extreme

A5. Bending to floor/pick up an object
○ None ○ Mild ○ Moderate ○ Severe ○ Extreme

A6. Walking on flat surface
○ None ○ Mild ○ Moderate ○ Severe ○ Extreme

A7. Getting in/out of car
○ None ○ Mild ○ Moderate ○ Severe ○ Extreme

A8. Going shopping
○ None ○ Mild ○ Moderate ○ Severe ○ Extreme

A9. Putting on socks/stockings
○ None ○ Mild ○ Moderate ○ Severe ○ Extreme

A10. Rising from bed
○ None ○ Mild ○ Moderate ○ Severe ○ Extreme

A11. Taking off socks/stockings
○ None ○ Mild ○ Moderate ○ Severe ○ Extreme

Quality of Life

Q1. How often are you aware of your hip problem?
○ Never ○ Monthly ○ Weekly ○ Daily ○ Constantly

Q2. Have you modified your life style to avoid potentially damaging activities to your hip?
○ Not at all ○ Mildly ○ Moderately ○ Severely ○ Totally

Q3. How much are you troubled with lack of confidence in your hip?
○ Not at all ○ Mildly ○ Moderately ○ Severely ○ Extremely

Q4. In general, how much difficulty do you have with your hip?
○ None ○ Mild ○ Moderate ○ Severe ○ Extreme

Subtotal: 0

Thank you very much for completing all the questions in this questionnaire.

Print page | Close Window | Reset

To save this data please print or Save As CSV

The HOOS Hip Survey Score is 0

Reference for Score: Klässbo M, Larsson E, Mannerkorpi E. Hip disability and osteoarthritis outcome score. An extension of the Western Ontario and McMaster Universities Osteoarthritis Index. Scand J Rheumatol. 2003;32(1):46-51. **Link**

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ANNEXURE 4

Participant Information Sheet

STUDY TITLE: Outcomes of core decompression with bisphosphonate versus bisphosphonate alone in patients with early osteonecrosis of the femoral head; a comparative observational study.

1. STUDY INVESTIGATORS:

Student: Dr, Ajitendra Pratap Singh, Junior Resident, Department of Orthopaedics

Guide: Dr Rehan Ul Haq, Professor, Head of Department, Department of Orthopaedics

Co-guides: Dr. Pankaj Kumar Mishra, Associate Professor, Department of Orthopaedics

Dr. Manish Dwivedi, Associate Professor, Department of Orthopaedics

2. Introduction:

We are conducting research to compare the clinical, radiological and patient-reported outcomes of core decompression with bisphosphonate versus bisphosphonate alone in patients with early osteonecrosis of the femoral head.

If you agree to take part voluntarily, we will ask you to sign a consent form.

3. Purpose of the study:

The aim of our study is to compare the clinical, radiological and patient-reported outcomes of core decompression with bisphosphonate versus bisphosphonate alone in patients with early osteonecrosis of the femoral head. Ours being a tertiary care institute most patients who presents with grade 1 or 2 osteonecrosis of femur head are already on some form of medical management especially bisphosphonates. All these patients are offered core decompression as a surgical option. However some of them refuse surgery. Hence, two groups are created; one core decompression with bisphosphonate and other who are taking bisphosphonate alone. However to the best of our knowledge there are no studies which have compared the clinical,

radiological and patient reported outcomes between these two groups

4. **Taking part** – what it involves:

a. Do I have to take part?

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Participation in this research is entirely voluntary. A decision to not take part, or to withdraw at any time, will not affect your rights or medical care in any way.

b. What is expected of me if I take part?

If you participate, we will take your medical history and examination. Radiological investigation including x-ray and MRI pelvis both hip will be done.

c. How long will my part in the study last?

Your participation in the study would be about six month follow up.

d. Do I have to come for extra visits or undergo extra investigations for the study?

Yes. Follow up at two weeks, 6 weeks , 3 months and 6 months extra visits needed.

e. What are the possible benefits in taking part

Your treatment would continue as per your discussion with the treating doctor.

There would be no specific benefits to you in taking part in this study.

f. What are the possible disadvantages and risks of taking part?

There are no foreseeable disadvantages or risks because of the study. There may be risk of loss of privacy and confidentiality of information collected even though all possible measures will be taken to ensure safe data storage and access.

g. What happens to the information collected from me?

All information collected will be kept strictly confidential. Results from the study will be reported as group data and will not identify you in any way. However, you may be identifiable from a photograph or other static or moving image, or from its legend or accompanying text in the published thesis or publication in a scientific journal.

h. What if I change my mind regarding participation in the study?

You are entitled to change your mind and withdraw at any time during the study without any disadvantage or penalty.

i. Whom do I contact for more information or if I have further questions or concerns?

I

If you want any information or have questions or concerns, you can contact:

Dr. Ajitendra Pratap Singh
Post graduate student,
Department of Othopaedics
Research
AIIMS, Bhopal
8383932412
Ajitendra1992@gmail.com

Dr. Shashank Purwar
Member Secretary,
Institute Ethics Committee – Student
(7773010099)
ihecpgr@aiimsbhopal.edu.in)

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ANNEXURE 4

प्रतिभागी सूचना पत्र

अध्ययन का शीर्षक: कुल्हे की हड्डी के सिर के शुरुआती ऑस्टियोनेक्रोसिस वाले रोगियों में बिस्फॉस्फोनेट के साथ कोर डी-कंप्रेशन बनाम अकेले बिस्फॉस्फोनेट के परिणाम; एक तुलनात्मक अवलोकन अध्ययन

अध्ययन जांचकर्ता - छात्र (नाम, विभाग): डॉ. अजितेंद्र प्रताप सिंह, जूनियर रेजिडेंट, ऑर्थोपेडिक्स विभाग, एम्स, भोपाल

1. **मार्गदर्शक (गाइड) (नाम, विभाग):** डॉ. रेहान उल हक, प्रोफेसर, ऑर्थोपेडिक्स विभाग, एम्स, भोपाल
2. **सह मार्गदर्शक/को-गाइड (नाम, विभाग):**
   डॉ. मनीष सिवेदी, एसोसिएट प्रोफेसर, ऑर्थोपेडिक्स विभाग, एम्स, भोपाल
   डॉ. डॉ. पंकज कुमार मिश्रा, एसोसिएट प्रोफेसर, ऑर्थोपेडिक्स विभाग, एम्स, भोपाल

2. परिचय:
हम कुल्हे की हड्डी के सिर के शुरुआती ऑस्टियोनेक्रोसिस वाले रोगियों में बिस्फॉस्फोनेट के साथ कोर डी-कंप्रेशन बनाम अकेले बिस्फॉस्फोनेट के नैदानिक, रेडियोलॉजिकल और क्लिनिकल परिणामों की तुलना करने के लिए अनुसंधान कर रहे हैं। यदि आप स्वेच्छा से भाग लेने के लिए सहमत हैं, तो हम आपसे एक सहमति पत्र पर हस्ताक्षर करने के लिए कहेंगे।

3. अध्ययन का उद्देश्य:
हमारे अध्ययन का उद्देश्य कुल्हे की हड्डी के सिर के शुरुआती ऑस्टियोनेक्रोसिस वाले रोगियों में बिस्फॉस्फोनेट के साथ कोर डी-कंप्रेशन बनाम अकेले बिस्फॉस्फोनेट के नैदानिक, रेडियोलॉजिकल और क्लिनिकल परिणामों की तुलना करना है। हमारा एक तृतीयक देखभाल संस्थान होने के नाते, अधिकांश रोगी हिप हेड के ग्रेड 1 या 2 ऑस्टियोनेक्रोसिस के साथ प्रस्तुत करते हैं, वे पहले से ही किसी न किसी रूप में चिकित्सा उपचार विशेष रूप से बिस्फॉस्फोनेट पर हैं। हालाँकि उनमें से कुछ इन्कार करते हैं। इसलिए, दो समूह बनाए गए हैं; बिस्फॉस्फोनेट के साथ एक कोर डी-कंप्रेशन और अन्य जो अकेले बिस्फॉस्फोनेट ले रहे हैं। हालाँकि, हमारी जानकारी के अनुसार ऐसा कोई अध्ययन नहीं है जिसने इन दो समूहों के नैदानिक, रेडियोलॉजिकल और क्लिनिकल परिणामों की तुलना की हो।

4. भाग लेना - इसमें क्या शामिल है:
a) **क्या मुझे भाग लेना है?**
इस शोध में भागीदारी पूरी तरह से स्वैच्छिक है। भाग न लेने का निर्णय, या बाद में भाग लेने का निर्णय आपके अधिकारों या चिकित्सा देखभाल को प्रभावित नहीं करेगा।

b) **यदि मैं भाग लेता हूँ तो मुझसे क्या अपेक्षा की जाएगी?**
यदि आप भाग लेते हैं, तो हम आपका मेडिकल इतिहास और परीक्षा लेंगे। एक्स-रे और एमआरआई दोनों की आवश्यकता होगी।

c) **अध्ययन में मेरी भागीदारी तक कितने समय तक चलेगा?**
अध्ययन में आपकी भागीदारी लगभग छह महीने की अवधि के लिए होगी।

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d) **क्या मुझे अतिरिक्त मुलाकात के लिए आना होगा या इसके लिए अतिरिक्त जांच-पड़ताल करनी होगी?**
हाँ। दो सप्ताह, 6 सप्ताह, 3 महीने और 6 महीने की अनुवर्ती यात्राओं की आवश्यकता होगी।

e) **भाग लेने के संभावित लाभ क्या हैं?**
इलाज करने वाले डॉक्टर के साथ आपकी स्थिति के अनुसार आपका इलाज जारी रहेगा। इस अध्ययन में भाग लेने से आपको कोई विशेष लाभ नहीं होगा।

f) **भाग लेने के संभावित नुकसान और जोखिम क्या हैं?**
अध्ययन के कारण कोई अनुमानित नुकसान या जोखिम नहीं हैं। एकत्र की गई जानकारी की गोपनीयता और गोपनीयता के नुकसान का जोखिम हो सकता है, भले ही सुरक्षित डेटा भंडारण और पहचान न छापने के लिए सभी संभव उपाय किए जाएं।

g) **मुझसे एकत्र की गई जानकारी का क्या होगा?**
एकत्र की गई सभी जानकारी को कड़ाई से गोपनीय रखा जाएगा। अध्ययन के परिणाम समूह डेटा के रूप में रिपोर्ट किए जाएंगे और किसी भी प्रकार से आपकी पहचान नहीं की जाएगी। हालाँकि, आप एक तस्वीर या अन्य दस्तावेज़ों में, या लेखों या वैज्ञानिक पत्रिकाओं में प्रकाशन में पहचाने जा सकते हैं।

h) **क्या होगा यदि मैं अध्ययन में भाग लेने के बारे में अपना विचार बदल दूँ?**
आप अध्ययन के दौरान किसी भी समय अपना विचार बदलने और वापस लेने के हकदार हैं बिना किसी नुकसान या दंड के।

i) **अधिक जानकारी के लिए मैं किससे संपर्क करूँ या यदि मुझसे कोई प्रश्न हैं?**
यदि आप कोई जानकारी चाहते हैं या आपके कोई प्रश्न या चिंताएँ हैं, तो आप संपर्क कर सकते हैं:
डॉ. अजितेंद्र प्रताप सिंह
स्नातकोत्तर छात्र, ऑर्थोपेडिक्स विभाग, एम्स, भोपाल
8383932412
ajitendra1992@gmail.com
डॉ. शशांक पुरवार
रजिस्ट्रार, संस्थान प्रशासन समिति - छात्र अनुसंधान
7773010099
ihecpgr@aiimsbhopal.edu.in

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प्रतिभागी सूचना सहमति प्रपत्र

[PARTICIPANT INFORMED CONSENT FORM (PICF)]

अध्ययन के लिए प्रतिभागी पहचान संख्या / Participant Identification Number for Study: ……..

अनुसंधान का शीर्षक / Title of Project : Outcomes of core decompression with bisphosphonate versus bisphosphonate alone in patients with early osteonecrosis of the femoral head; a comparative observational study

छात्र शोधकिाष का नाम / Name of Student Investigator : Dr Ajitendra Pratap Singh
शोध मागषदशषक का नाम / Name of Thesis Guide : Dr Rehan Ul Haq

मैंने संस्करण संख्या II…… दिनांक 20-08-2022 के सूचना पत्रक में दिए गए सभी बिंदुओं को सावधानीपूर्वक पढ़ लिया है। मुझे अपनी भाषा में स्पष्ट रूप से विस्तृत रूप से समझा दिया गया है, और मैंने बिंदुओं को पूरी तरह से समझ लिया है। मैं पुष्टि करता हूँ कि मुझे सवाल पूछने का अवसर मिला है। The contents of the information sheet version II dated 20th August 2022 that was provided have been read carefully by me / explained in detail to me, in a language that I comprehend, and I have fully understood the contents. I confirm that I have had the opportunity to ask questions.

मुझे इस अध्ययन की प्रकृति एवं उद्देश्य और इसके संभावित जोखिमों/लाभों तथा अध्ययन की अनुमानित अवधि एवं अन्य प्रासंगिक जानकारी के बारे में विस्तारपूर्वक समझा दिया गया है। मुझे बताया गया है कि इस अध्ययन में मेरी भागीदारी स्वैच्छिक है और मैं इस अध्ययन से किसी भी समय बिना कोई कारण बताए, अपना नाम वापस लेने के लिए स्वतंत्र हूँ। नाम वापस लेने पर मेरी चिकित्सा देखभाल या कानूनी अधिकारों पर कोई प्रभाव नहीं पड़ेगा। The nature and purpose of the study and its potential risks/benefits and expected duration of the study, and other relevant details of the study have been explained to me in detail. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal right being affected.

मैं समझता/समझती हूँ कि इस अनुसंधान में मेरी भागीदारी से मेरे बारे में एकत्र की गई जानकारी और मेरे चिकित्सा दस्तावेजों के किसी भी भाग को एम्स के जिम्मेदार व्यक्तियों द्वारा ही देखा जाएगा। मैं इन व्यक्तियों को मेरे रिकॉर्ड प्राप्त करने की अनुमति देता/देती हूँ। I understand that the information collected about me from my participation in this research and sections of any of my medical notes may be looked at by responsible individuals from AIIMS. I give permission for these individuals to have access to my records.

यदि प्रतिभागी बच्चा है, तो उसकी मौखिक या लिखित सहमति प्राप्त की गई है। If participant is child, his / her verbal or written assent has been obtained.

मैं इस अध्ययन में भाग लेने के लिए सहमति देता/देती हूँ। I agree to take part in the above study.

_____

(प्रतिभागी के हस्ताक्षर / बांए अंगूठे का निशान) (Signature / Left Thumb Impression)

दिनांक /Date..... स्थान/Place .....

प्रतिभागी का नाम/Name of the participant .....

पुत्र/पुत्री/पत्नी का नाम /Son/Daughter/Spouse of…….

पूरा पोस्टल पता /Complete Postal Address .....

अगर अशिक्षित हो / *If illiterate,*

सूचना पत्र को प्रतिभागी को पढ़ा और समझाया गया है, और प्रश्न पूछने का अवसर दिया गया है। मैं पुष्टि करता/करती हूँ कि व्यक्ति ने स्वतंत्र रूप से सहमति दी है।

The information sheet has been read and explained to the participant, and given the opportunity to ask questions. I confirm that the individual has given consent freely.

कानूनी रूप से स्वीकृत प्रतिनिधि अथवा निष्पक्ष गवाह के हस्ताक्षरSignature of Legally Acceptable Representative or impartial witness:

दिनांक / Date:

प्रतिनिधि अथवा निष्पक्ष गवाह का नाम / Name of LAR or impartial witness:

पता /Address:

प्रमाणित किया जाता है कि उक्त सहमति मेरी उपस्थिति में प्राप्त की गई।This is to certify that the above consent has been obtained in my presence.

_____

छात्र शोधकर्ता के हस्ताक्षर दिनांक

…….. स्थान……

Signature of the Student Investigator Date …… Place .....

कृपया ध्यान दें: सहमति प्रपत्र तीन प्रतियों में (1) रिसर्चर के लिए, (2) शिक्षक के लिए, (3) संस्थान के लिए तैयार करें।

Please note: Three copies should be made, for (1) Patient, (2) Researcher, (3) Institution

ANNEXURE 5

Master sheet of group A

S.NO.	AGE	SEX	Surgical Procedure	Sugery Date	Pescraitme nt Date	Grading (at Day 0)						Day 0 (Pre-intervention)						2 WEEKS		3 MONTHS						6 MONTHS							
						FICAT AND ARLET		AVN GRADE (ARCO)		JIC		VAS (DAY 0)		HHS (DAY 0)		HOOS (DAY 0)		VAS (2 WEEKS)		VAS (3 MONTHS)		HHS (3 MONTHS)		HOOS (3 MONTHS)		FICAT AND ARLET (6 MONTHS)		VAS (6 MONTHS)		HHS (6 MONTHS)		HOOS (6 MONTHS)	
						Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
1	22Y	M	BILATERAL CD	19-01-23	19-01-23	2	3	2	3	A	C2	II	7	100	63.8	100	46.9	0	4	5	4	79.8	69.8	67.5	56.9	3	3	7	6	63	59.8	67.5	51.2
2	35Y	M	RIGHT CD	07-02-23	07-02-23	2	3	2	3	C1	C1	II		49		10.1		10		8		42.75		56		3	3	8		42.9		47.5	
3	30Y	M	LEFT CD	09-02-23	09-02-23		2		2		C2		7		50.9		50.2		7		9		38.3		38.8		3	GOT THR LEFT SIDE IN OCT 2023						
4	38Y	M	RIGHT CD	02-03-23	02-03-23	2	1	2	1	A	A	II		72		66.3		5		5		68.4		66.3		2	2	4		68.4		66.3	
5	29Y	M	LEFT CD	16-03-23	16.03.2023	3	2	3	2	A	A		II		100		100		II		II		100		100	3	2		0		100		100
6	44Y	M	LEFT CD	14-03-23	14-03-23	2	2	3	2	C1	C2		6		49.95		50.6		4		2		96		67.5	3	2		2		83.8		71.9
7	55Y	M	LEFT CD	21-03-23	21.03.2023	3	2	3	2	C1	B		6		83		78.8		4		4		92.9		85.6	3	2		4		92.9		85.6
8	28Y	M	BILATERAL CD	19-07-22	19.07.2022	1	2	1	2	A	C2	10	18	44.7	44.7	52.6	52.6	6	6	3	3	78.8	78.8	74.2	74.2	2	2	3	3	78.8	78.8	74.2	74.2
9	24Y	F	BILATERAL CD	22-09-23	22-09-23	2	1	2	1	C2	B	6	II	63.8	100	62.5	100	4	II	2	II	91	100	88.8	100	2	2	4	2	78.8	91.8	75	86.6
10	25Y	F	BILATERAL CD	03-05-23	03-05-23	2	2	2	3	C1	C2	II	5	100	72.56	100	76.9	0	4	0	4	100	66.8	100	58.2	2	3	4	8	78	54.8	62.5	31.9
11	28Y	M	LEFT CD	20-04-23	20-04-23		2		2		A		6		81		78.8		5		4		92.9		85.6		2		3		92.9		85.6
12	36Y	M	BILATERAL CD	03-05-23	03-05-23	2	2	2	2	C2	C1	II	II	42.6	42.6	51.9	51.9	6	6	6	6	64.6	64.6	71.8	72.8	3	3	6	6	64.6	64.6	71.8	72.8
13	26Y	M	BILATERAL CD	15-05-23	15.05.2023	2	2	2	2	C2	C2	5	5	75	75	68.2	68.2	4	4	7	7	63.8	63.8	58.6	58.6	2	2	7	7	63.8	63.8	58.6	58.6
14	54Y	M	BILATERAL CD	09-06-23	09-06-23	3	2	3	2	C2	C2	7	4		78.9		76.9	7	4	GOT THR RIGHT SIDE ON MAY 2024														
15	31Y	M	BILATERAL CD	03-08-23	03-08-23	2	2	2	2	A	B	II	II	61.9	61.9	65.6	65.6	6	4	6	4	61.9	48	75.6	61.5	2	2	6	4	61.9	48	75.6	61.5
16	26Y	F	RIGHT CD	06-05-23	06-05-23	2		2		A		8		78		56.25		4		4		90.9		80.6		2		4		90.9		80.6	
17	29Y	F	BILATERAL CD	28/11/2023	28/11/2023	2	2	3	2	B	B	9	7	60.6	71	42.5	61.3	6	6	5	4	68	78	59.4	76.9	3	2	5	4	68	78	59.4	76.9
18	28Y	F	BILATERAL CD	12-04-23	12-04-23	2	2	2	2	A	A	II	9	100	34.8	100	25	0	6	0	4	100	96	100	94	2	2	0	4	100	96	100	94
19	41Y	F	BILATERAL CD	26-12-23	26-12-23	2	3	2	3	C1	C2	6		62.8		68.8		6		5		71		75.6		2	4	5		71		75.6	
20	25Y	M	BILATERAL CD	08-02-24	08-02-24	2	2	2	3	B	B	II	7	100	66	100	62.5	0	4	0	4	100	79	100	75	2	2	0	4	100	79	100	75
21	40Y	M	BILATERAL CD	07-02-24	07-02-24	2	2	2	3	B	C1	II	6	100	78	100	62.5	0	4	0	4	100	88	100	84	2	2	0	4	100	88	100	84
22	42Y	M	BILATERAL CD	03-04-24	03-04-24	2	2	3	2	C2	C1	7	0	92.7	100	51.2	100	4	0	4	0	71.7	100	75.6	100	3	2	4	0	71.7	100	75.6	100
23	54Y	F	BILATERAL CD	18-04-24	18-04-24	2	2	2	2	B	B	II	8	72	72	66.3	66.3	5	5	5	5	68.4	68.4	66.3	66.3	2	2	5	5	68.4	68.4	66.3	66.3
24	30Y	M	BILATERAL CD	19-04-24	19-04-24	2	2	2	2	C2	C2	II	4	100	80	100	74.4	II	2	II	2	100	91	100	78.1	2	2	0	2	100	91	100	78.1
25	21Y	F	BILATERAL CD	11-08-23	11-08-23	2	2	2	2	C2	C1	7	0	49.7	100	53.1	100	4	II	5	4	64.7	77	73.8	75	3	2	5	4	64.7	77	73.8	75
26	23Y	F	BILATERAL CD	30-01-24	30-01-24	2	3	2	3	C1	C1	5		76		59.4		4		4		93		75.6		2	3	4		93		75.6	

ANNEXURE-6

Master sheet of group B

				Grading (at Day 0)						Day 0 (Pre-intervention)						2 WEEKS		3 MONTH						6 MONTH					
UNO	AGE	SEX	Recruitment Date	FICAT AND ABLET		AVD GRADE (ABCD)		DC		VAS (DAY 0)		HER (DAY 0)		HOOR (DAY 0)		VAS (2 WEEKS)		VAS (3 MONTH)		HER (3 MONTH)		HOOR (3 MONTH)		FICAT AND ABLET (6 MONTH)		VAS (6 MONTH)		HER (6 MONTH)		HOOR (6 MONTH)	
				Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
1	18Y	M	20-06-23	2	2	2	2	C1	C1	7	7	61.9	61.9	56.3	56.3	4	4	4	4	81	81	81.3	81.3	2	2	5	5	71	71	75.6	75.6
2	36Y	M	26-05-23	2		2		A		8		50		62.5		2		2		96		87.5		2		2		96		87.5	
3	33Y	M	10-06-23	2	2	2	2	A	A	5	5	68	68	75	75	4	4	4	4	81	81	80.6	80.6	2	2	4	4	81	81	80.6	80.6
4	27Y	M	20-06-23	2	3	2	3	B	C1	6		69.8		55.6		4		4		76		80		2	3	4		79		81.3	
5	21Y	F	15-08-23	2	3	2	3	A	B	6		56.8		43.5		3		3		79		81.3		2	3	3		79		81.3	
6	46Y	M	25-07-23	2	2	2	3	C1	C2	4	8	86	43.3	78.8	44.4	3	4	4	4	72	72	80	80	2	3	4	4	74	74	80	80
7	36Y	F	10-06-23	2	2	2	2	c1	c2	6	6	54.9	54.9	46.3	46.3	4	4	5	5	93.8	93.8	56.3	56.3	2	2	3	3	93	93	88.8	88.8
8	34Y	M	28-06-24		2		2		C2		7		55		47.5		5		5		68		74.4		2		5		68		74.4
9	36Y	M	05-08-23	2	2	2	3	B	B	6	6	60.9	60.9	71.9	71.9	4	4	4	4	74	74	77.5	77.5	2	3	5	5	72	72	75	75
10	22Y	M	17-10-23	2	2	2	2	A	B	7	7	56.8	56.8	53.5	53.5	5	5	3	3	84	84	78.1	78.1	2	2	3	3	84	84	78.1	78.1
11	43Y	M	01-04-24	2	2	3	2	c1	b	6	0	43.8	100	56.9	100	4	0	5	0	63.6	100	76.9	100	3	2	5	0	63.6	100	76.9	100
12	44Y	M	22-11-23	2	2	2	3	C1	C1	8	10	35	25	44.4	56.5	6	6	4	6	72	63.8	78.1	56.3	2	3	4	6	72	63.8	78.1	56.3
13	56Y	M	26-10-24	3	2	3	3	C2	C2		8		39.8		35.6		4		4		78		76.9	3	2		4		78		76.9
14	57Y	M	01-10-24	2	2	2	2	C1	B	0	6	100	66	100	47.5	0	4	0	4	100	76	100	77.5	2	2	0	4	100	76	100	77.5
15	36Y	M	12-10-24	2	3	2	3	A	B	4		61		63.9		2		2		92		87.5		2	3			92		87.5	
16	26Y	M	26-12-23	2		2		A		8		45.3		78.4		5		2		94		88.1		2		2		94		88.1	
17	59Y	M	12-07-23	2	2	3	2	C2	A	8	0	42.5	100	40	100	6	0	5	0	62.8	100	55	100	2	3	5		62.8	100	55	100
18	21Y	M	25-08-23	2		2		C1		4		78		66.9		4		4		77		66.9		2		4		77		66.9	
19	58Y	M	03-07-24	2		2		C2		5		60.8		75.6		5		5		60.8		75.6		2		7		42.3		43.9	
20	45Y	M	16-04-24	2	1	2	1	A	A	6	0	45.8	100	56.9	100	3	0	3	0	92	100	84.4	100	2	1	3	0	92	100	84.4	100
21	24Y	M	20-04-24	2	3	2	3	C2	C2	8		59.5		43.1		6		4		72		78.4		2	3	4		72		78.4	
22	31Y	F	20-04-24	4	2	4	2	C2	B		0		100		100		0		0		100		100	4	2		0		100		100
23	31Y	F		4	2	4	2	B	A		4		79		78.4		2		2		92		85.6	4	2		2	92		85.6	
24	57Y	M	08-04-24	2	2	2	3	C1	C1	5	8	79	43.3	62.5	56.3	4	5	4	4	76	76	78.4	78.4	2	2	4	4	76	76	78.4	78.4
25	41Y	M	18-04-24	1	2	1	2	A	A	0	7	100	43.9	100	44.4	0	4	0	3	100	92	100	85.6	1	2	0	3	100	92	100	85.6
26	45Y	M	28-04-24	3	2	3	2	C1	B		6		68.8		56.3		4		2		84		88.8	3	2		2		84		88.8
27	22Y	M	10-04-24	2	2	3	2	C1	A	8	6	44	43.8	44.4	56.9	5	3	4	2	76	92	78.1	87.5	2	2	4	2	76	92	78.1	87.5
28	61Y	F	16-04-24	2	4	2	4	A	B	4		74		76.9		2		2		74		76.9		2	4	2		74		76.9	
29	51Y	M	13-07-23	2	2	3	2	C1	C1	6	0	62.8	100	56.3	100	4	0	4	0	78	100	78.1	100	2	2	5	2	75	96	75.6	87.5
30	26Y	M	04-04-24	2	3	2	3	B	C1	5		65.6		75.6		4		2		89		88.8		2	3	2		89		88.8	